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CANTOX ENVIRONMENTAL

DELORO VILLAGE
EXPOSURE ASSESSMENT AND HEALTH RISK CHARACTERIZATION FOR ARSENIC AND OTHER METALS

- FINAL REPORT -

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DELORO VILLAGE
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EXECUTIVE SUMMARY

The Village of Deloro, located on the Moira River in southeastern Ontario and home to a population of 140 people, is the focus of an extensive risk assessment and remediation effort by the Ontario Ministry of the Environment (OMOE). The village is located along the property line of a former mine and refinery, and contamination of the former mine site and the village of Deloro is the result of a century of these mining and refining activities. The current effort is aimed at quantifying and mitigating exposures and risks to the residents of Deloro which are associated with the contamination of the former mine site by heavy metals and radiological agents and the subsequent emission of contaminants from the mine site via liberation of dusts, volatilization, and/or leaching into the Moira River watershed. The OMOE conducted a screening level risk assessment on the contaminated soils of the village of Deloro, and have identified several heavy metals (arsenic, cobalt, lead, nickel and silver) as well as radiological agents as being of potential health concern to residents.

Under the leadership of OMOE and CH2M Gore & Storrie Limited (CGS), CANTOX ENVIRONMENTAL INC. has conducted an exposure assessment and health risk characterization for the residents of Deloro, Ontario, based on concentrations of arsenic, cobalt, lead, nickel and silver in the air, water, soil, and food throughout the village.

The objectives of this assessment were as follows:

(i) to review the exposures and/or risks posed to the public in the vicinity of other mining or smelting operations in North America;

(ii) to review the sources and levels of exposure of chemicals of concern to typical Ontarians, including home grown and market basket foods, soils, drinking water, and air;

(iii) to determine if the concentrations of arsenic and the other metals of concern in various media in Deloro would pose a risk of adverse health effects for adults and children dwelling in the village, and to compare results to exposures in other mining/smelter areas as well as exposures of typical Ontario residents;

(iv) to compare the results of exposure assessment to those of biological monitoring efforts (specifically urinary arsenic determinations); and,

(v) review various options of exposure and risk mitigation and make estimates of possible risk reductions.

Review of Exposure to Arsenic

Arsenic is a naturally-occurring element which is found in terrestrial and aquatic environments, which is capable of extensive cycling through both biotic and abiotic components of these systems. Therefore, while exposures to arsenic may be exacerbated by human activity such as mining (*i.e.*, point sources), even populations without direct contact with such point sources will be exposed to arsenic at some level. Environment Canada has estimated that the total average daily intake of inorganic arsenic by Canadians without direct contact to point sources ranges from 0.1 to 2.6 µg/kg body weight/day, with the greatest exposure occurring in infants and young children. The OMOE examined the relative contribution of various pathways of exposure to total daily intake of inorganic arsenic via ingestion for Ontario residents, and identified as major contributors both food (84%) and drinking water (15%). Soil/dust ingestion pathways contributed less than 1% to the total. Environment Canada estimated daily intakes of inorganic arsenic by Canadians living near point sources of arsenic contamination, from all exposure pathways, to range from <0.1 to 35 µg/kg body weight/day, with the greatest exposure occurring in infants and young children.

Analysis of concentrations of arsenic compounds in the urine is considered to be a reliable, non-intrusive technique for evaluating recent arsenic exposure, and thus serves as an indicator of the health status of populations exposed to arsenic. Total urinary arsenic concentrations reflect intakes of all forms of arsenic, including inorganic arsenic (considered to be responsible for toxicological effects associated with arsenic) as well as organic arsenicals (which are considered to be without significant toxicological effects). Therefore, speciated arsenic measurements, reflecting concentrations of only inorganic forms of arsenic and their metabolites (arsenic III, arsenic V, monomethylarsonic acid and dimethylarsonic acid) are generally considered the appropriate measure for use in health assessment. Populations not exposed to a point source of arsenic have average urinary speciated arsenic concentration of about 8 µg/L, in comparison to 52 µg/L reported for populations in the vicinity of mining or smelting operations, and 233 µg/L in populations exposed to arsenic occupationally or via high endemic concentrations in drinking water.

Exposure and Risk Assessment Results

The human health risk assessment was undertaken in order to characterize the risks posed to receptors of all age classes (infant, preschool child, child, adolescent and adult) by exposures via all relevant pathways (oral, inhalation or dermal contact with air, water, soil, dust and food). The exposure pathways considered in the risk assessment are shown in Figure 1. Two analytical techniques were used to assess risk in the Village of Deloro: deterministic and probabilistic analyses. In a fully deterministic analysis, single values, or point estimates, were used for parameters describing exposure and toxicity. Because these point estimates were typically selected to maximize exposure and risk, the deterministic analysis can be considered to be a "worst-case" assessment. In probabilistic analysis, probability distributions were assigned to the exposure or risk parameters used in the assessment and the risk estimates were expressed as cumulative distribution functions.

Risk characterization, the final step in risk assessment, consists of either a comparison of estimated exposures to an acceptable level of risk or exposure. For non-carcinogenic chemicals the acceptable is the toxicological criteria, and the comparison may be expressed as an Exposure Ratio [ER]. For carcinogenic chemicals, risks are expressed as Cancer Risk Levels (CRLs), and a comparison is made to acceptable levels of incremental cancer risk. Negligible cancer risk levels are generally considered to be $1x10^{-4}$ to $1x10^{-6}$, but evaluation of predicted cancer risks for a population must also consider predicted risks for a background or "typical" population, since "typical" populations are considered to be without undue cancer risks, predicted CRLs for these receptors can provide a valid "acceptable level" of risk. In cases where the estimated exposures or risks are less than the acceptable level, it can be concluded that there would be no risk of adverse health effects. When estimated exposures or risks exceed the acceptable level, consideration must be given to the possibility of adverse health effects, but such exceedences are not necessarily indicative of potential risks, but may reflect overestimation of risk due to the use of overly conservative estimates (*e.g.,* overestimating exposures through use of maximum soil ingestion rates). When evaluating risks, deterministic analyses were used initially, to characterize the plausible maximum ("worst-case") and typical mean exposures experienced by Deloro residents. In cases where the potential for measurable risks were indicated by comparison to the criteria and to risks of typical Ontario residents, it was concluded that a more rigorous and realistic evaluation of risks should be conducted through probabilistic analysis. The various uncertainties associated with each phase of the risk assessment were examined in order to ensure that the risk characterization would be both conservative and realistic. In all cases, the discussion and analysis of results focused on the most sensitive receptor (composite for carcinogens and infant or preschool child for non-carcinogens).

Arsenic (Carcinogenic)

The composite receptor, representing cumulative exposure over a lifetime, had the highest probabilistic cancer risk levels (CRLs). The predicted total cancer risk levels for the residents of Deloro, with and without consumption of home garden produce, were slightly higher than those predicted for typical Ontario residents (Tables 1 & 2; Figure 2, 3 & 4). Estimated maximum cancer risks are about 0.2 times higher than those for typical Ontario residents (95^{th} percentiles: 0.912 per 1000 versus 0.817 per 1000). Deloro-related exposures contributed less than 0.1 per 1000 to this risk.

TABLE 1 Arsenic Lifetime Cancer Risk Levels (ALL CANCERS) for Home Garden Consumers

	CANCER RISK LEVEL				
	DETERMINISTIC		PROBABILISTIC		
	plausible maximum	typical average	5th percentile	median	95th percentile
TYPICAL ONTARIO					
TYPICAL ONTARIO RESIDENT	1.42e-03	2.56e-04	3.19e-04	5.37e-04	8.17e-04
DELORO ALONE					
WHOLE TOWN	4.09e-04	1.14e-04	6.57e-05	1.09e-04	1.79e-04
ZONE 1	1.42e-04	8.37e-05	4.83e-06	8.15e-05	1.44e-04
ZONE 2	1.75e-04	9.08e-05	5.42e-05	8.85e-05	1.55e-04
ZONE 3	3.97e-04	1.25e-04	7.52e-05	1.34e-04	2.30e-04
ZONE 4	4.89e-04	1.51e-04	7.84e-05	1.30e-04	2.06e-04
DELORO INCLUDING BACKGROUND					
WHOLE TOWN	1.71e-03	3.51e-04	4.02e-04	6.27e-04	9.12e-04
ZONE 1	1.44e-03	3.21e-04	3.74e-04	6.02e-04	8.86e-04
ZONE 2	1.47e-03	3.28e-04	3.77e-04	6.11e-04	8.90e-04
ZONE 3	1.69e-03	3.62e-04	4.28e-04	6.61e-04	9.40e-04
ZONE 4	1.79e-03	3.89e-04	4.14e-04	6.41e-04	9.32e-04

TABLE 2 Arsenic Lifetime Cancer Risk Levels (ALL CANCERS) for non-Home Garden Consumers

	CANCER RISK LEVEL				
	DETERMINISTIC		PROBABILISTIC		
	plausible maximum	typical average	5th percentile	median	95th percentile
TYPICAL ONTARIO					
TYPICAL ONTARIO RESIDENT	1.41e-03	2.53e-04	3.08e-04	5.39e-04	8.23e-04
DELORO ALONE					
WHOLE TOWN	3.83e-04	1.07e-04	5.95e-05	9.84e-05	1.68e-04
ZONE 1	1.39e-04	8.20e-05	4.76e-05	7.91e-05	1.43e-04
ZONE 2	1.70e-04	8.79e-05	5.08e-05	8.42e-05	1.51e-04
ZONE 3	3.77e-04	1.18e-04	6.82e-05	1.16e-04	1.99e-04
ZONE 4	4.65e-04	1.38e-04	7.29e-05	1.16e-04	1.88e-04
DELORO INCLUDING BACKGROUND					
WHOLE TOWN	1.68e-03	3.44e-04	3.84e-04	6.23e-04	9.08e-04
ZONE 1	1.44e-03	3.19e-04	3.71e-04	5.95e-04	8.77e-04
ZONE 2	1.47e-03	3.25e-04	3.76e-04	6.04e-04	8.83e-04
ZONE 3	1.67e-03	3.53e-04	4.11e-04	6.36e-04	9.19e-04
ZONE 4	1.76e-03	3.75e-04	4.13e-04	6.31e-04	9.19e-04

In the evaluation of specific cancer types (Table 3), it is apparent that the CRLs for lung cancer are significantly lower than that for skin cancer, indicating that the majority of the total cancer risk is due to risk of skin cancer (>99.95%). In addition, the predicted CRLs for lung cancer for Deloro residents were lower than those for Ontario residents, further supporting the conclusion that risks associated with exposure to Deloro-specific media are primarily, if not entirely, due to risk of skin cancer.

TABLE 3 Incremental Arsenic Lifetime Cancer Risk Levels (by cancer type) for Whole Town

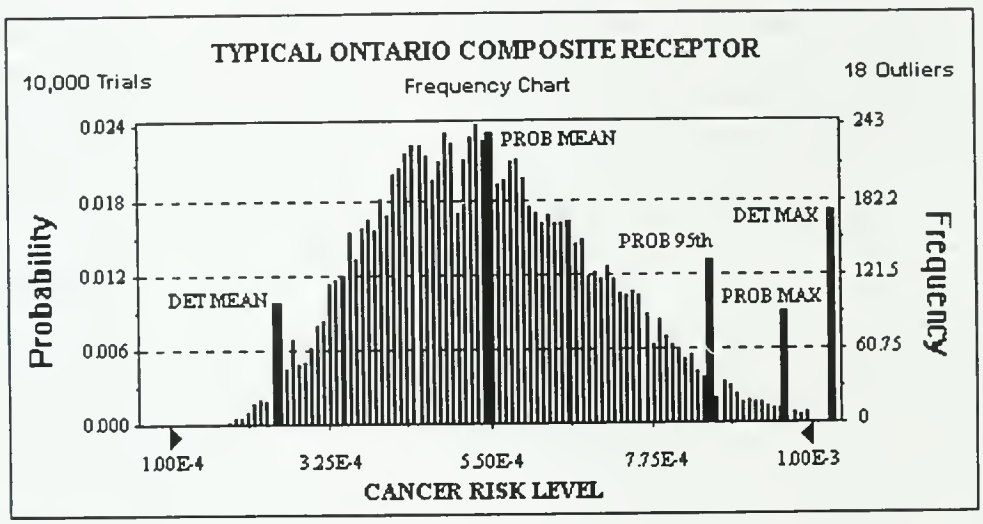
	CANCER RISK LEVEL				
	DETERMINISTIC		PROBABILISTIC		
	plausible maximum	typical average	5th percentile	median	95th percentile
ALL CANCERS COMBINED					
Typical Ontario resident	1.42e-03	2.56e-04	3.19e-04	5.37e-04	8.17e-04
Deloro alone (no home garden consumption)	3.83e-04	1.07e-04	5.95e-05	9.84e-05	1.68e-04
Deloro alone (home garden consumption included)	4.09e-04	1.14e-04	6.57e-05	1.09e-04	1.79e-04
Deloro including home garden consumption & background contribution	1.71e-03	3.51e-04	4.02e-04	6.27e-04	9.12e-04
LUNG CANCERS					
Typical Ontario resident	2.81e-05	2.75e-06	2.94e-06	1.00e-05	1.89e-05
Deloro alone (no home garden consumption)	4.38e-07	1.75e-07	1.69e-07	3.76e-07	7.39e-07
Deloro alone (home garden consumption included)	4.38e-07	1.75e-07	1.69e-07	3.76e-07	7.39e-07
Deloro including home garden consumption & background contribution	3.94e-06	1.17e-06	1.04e-06	2.83e-06	5.28e-06
SKIN CANCERS					
Typical Ontario resident	1.39e-03	2.53e-04	3.04e-04	5.20e-04	8.02e-04
Deloro alone (no home garden consumption)	3.83e-04	1.07e-04	3.93e-05	9.81e-05	1.68e-04
Deloro alone (home garden consumption included)	4.08e-04	1.14e-04	6.48e-05	1.07e-04	1.83e-04
Deloro including home garden consumption & background contribution	1.70e-03	3.50e-04	3.92e-04	6.14e-04	9.10e-04

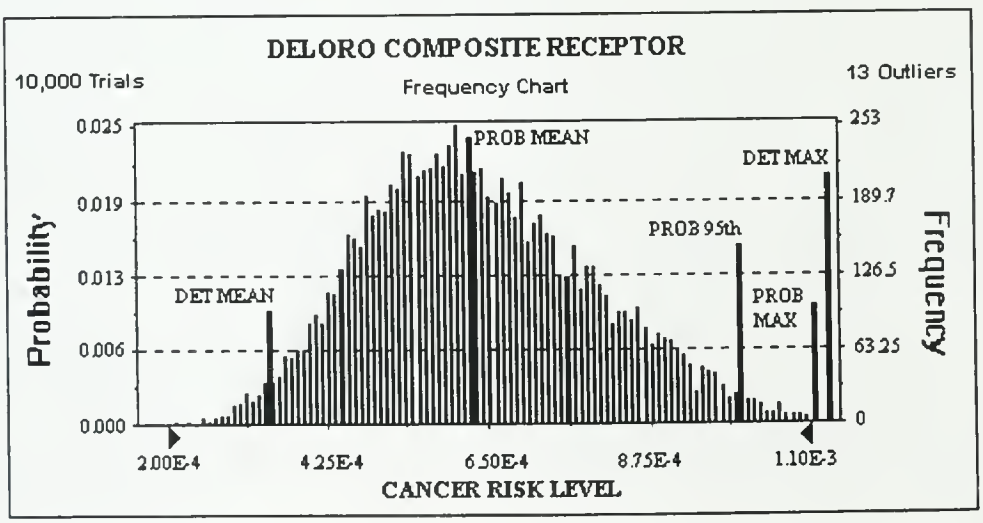
A detailed examination of the contributors to overall predicted skin cancer risks from arsenic for Deloro residents (consuming home garden produce) indicated that the general food basket common to all Ontarians were responsible up to 80% of overall exposures (Figures 5 & 6) and risks (Figure 7). The Deloro-related pathway making the greatest contribution to risks of Deloro residents was consumption of municipal drinking water. The concentrations of arsenic in drinking water in Deloro were well below Ontario drinking water objectives for safety. Exposures through consumption of home garden produce, as well as dermal contact and ingestion of soil and dust ingestion were minimal (1.5% for garden produce, and 4% for all direct soil/dust pathways).

Negligible or *de minimis* cancer risk level is generally considered to be 1 in ten thousand ($1x10^{-4}$) to 1 in one million ($1x10^{-6}$), and risk estimates for a population which are greater than this level would be considered to be elevated. However, when estimates of cancer risk for typical Ontario residents exceed this negligible level of risk, it would be expected that the estimated risks for any population within Ontario, such as the residents of Deloro, would also exceed the level considered negligible. This is evident in the current assessment, as the probabilistic CRLs for typical Ontario residents ranged from $3.19x10^{-4}$ to $8.17x10^{-4}$ (5^{th} to 95^{th} percentiles), while CRLs for Deloro residents ranged from $4.02x10^{-4}$ to $9.12x10^{-4}$, higher than typical Ontario by a factor of about 0.2-fold. The elevation of risk for typical Ontario residents would indicate an overestimation of risk due to a high degree of conservatism in the risk assessment; the elevation of risks to Deloro residents, in large part, would be due to the same conservatism. Of considerable importance to the assessment of arsenic is the conservatism inherent in the dose-response relationship used in development of the cancer potency factor for arsenic by the U.S. EPA. This conservatism would result in the overestimation of the potency of arsenic in inducing skin cancer, and consequently may lead to overestimation of predicted skin cancer risks, especially at lower rates of exposure more typical of most North American populations. To summarize briefly, the U.S. EPA cancer potency is based on an epidemiological study of skin cancer in a Taiwanese population, and limitations in using these data include uncertainties in actual exposure levels, nutritional status and other factors affecting susceptibility to toxicity. Recently derived cancer potency factors based on cancers at other sites in the body (*e.g.*, the bladder) are similarly hampered by limitations in the data. In the frame of reference of the current assessment, if the skin cancer potency of arsenic has been overestimated, then the risks of skin cancer predicted for the population of Deloro or Ontario would also have been overestimated in this assessment. Therefore, given that the same methodologies were used in estimating exposure and risk for typical Ontario residents and Deloro residents, the comparison of these two groups would be the most appropriate way of evaluating the risk estimates. Given that based on actual cancer risk estimates, the typical Ontario resident is not considered to be at elevated risk of cancer from arsenic, the predicted risk for this population can provide a reference by which risks to Deloro residents may be evaluated, as has been done above.

The following forecast charts are examples of the probability density function (PDF) characterizing the distribution of CRLs for carcinogenic arsenic risks for the composite receptor of Ontario and Deloro, following 10,000 iterations of the probabilistic model. The forecast chart demonstrates the actual shape of the distribution of risk estimates. PDFs for

the other probabilistic modelling results (all receptors, arsenic and lead, home garden consumers and non-consumers) have a similar shape, as can be seen in comparing the distributions for Ontario and Deloro composite receptors (below). These results demonstrate that for both Ontario and Deloro residents, the 95th percentile of the risk estimate, which is typically used as the decision point in probabilistic risk assessments, is representative of only a very small segment of the population. In comparison, the risk estimates for the bulk of the population, which fall around the 50th percentile, tend to be much lower that the 95th percentile. As would be expected, based on the discussion of results earlier, the cancer risk estimates for Ontario residents are slightly lower than those for Deloro residents, which is reflected in the minor shift of the typical Ontario distribution curve to the left.





Arsenic (Non-Carcinogenic)

The maximum deterministic exposure estimates for Deloro residents and typical Ontarians exceeded the toxicological criterion, which was based on adverse effects on the skin, with and without consumption of home garden produce (see Tables 4, 5 & 6). The highest estimated risk values were observed for infants and preschool children in Deloro (mean and maximum ER values of 1.57 and 10 for preschool children without home garden consumption), while estimates for typical Ontario residents of the same age classes were lower by a factor of 1.6-fold (mean and maximum ER values of 1.02 and 6.97 for preschool children). The observed ERs indicated marginal exceedences of the toxicological criterion; however, because there were exceedences, and because risk estimates for residents of Deloro exceeded those predicted for typical Ontario residents, arsenic was retained for probabilistic analysis based on non-carcinogenic endpoints.

TABLE 4 Arsenic (Non-Carcinogenic) Long Term Exposure Ratio Values (preschool child) for Home Garden Consumers

	EXPOSURE RATIO VALUES				
	DETERMINISTIC		PROBABILISTIC		
	plausible maximum	typical average	5th percentile	median	95th percentile
TYPICAL ONTARIO					
TYPICAL ONTARIO RESIDENT	6.97	1.02	0.745	2.35	5.15
DELORO ALONE					
WHOLE TOWN	3.63	0.640	0.203	0.508	1.29
ZONE 1	1.29	0.44	0.137	0.369	0.991
ZONE 2	1.58	0.487	0.152	0.401	1.04
ZONE 3	3.53	0.707	0.248	0.669	1.63
ZONE 4	4.34	0.884	0.268	0.631	1.47
DELORO INCLUDING BACKGROUND					
WHOLE TOWN	10	1.57	1.15	2.87	5.63
ZONE 1	7.66	1.37	1.02	2.75	5.52
ZONE 2	7.96	1.41	1.09	2.75	5.53
ZONE 3	9.9	1.63	1.26	2.99	5.85
ZONE 4	10.7	1.81	1.23	2.95	5.87

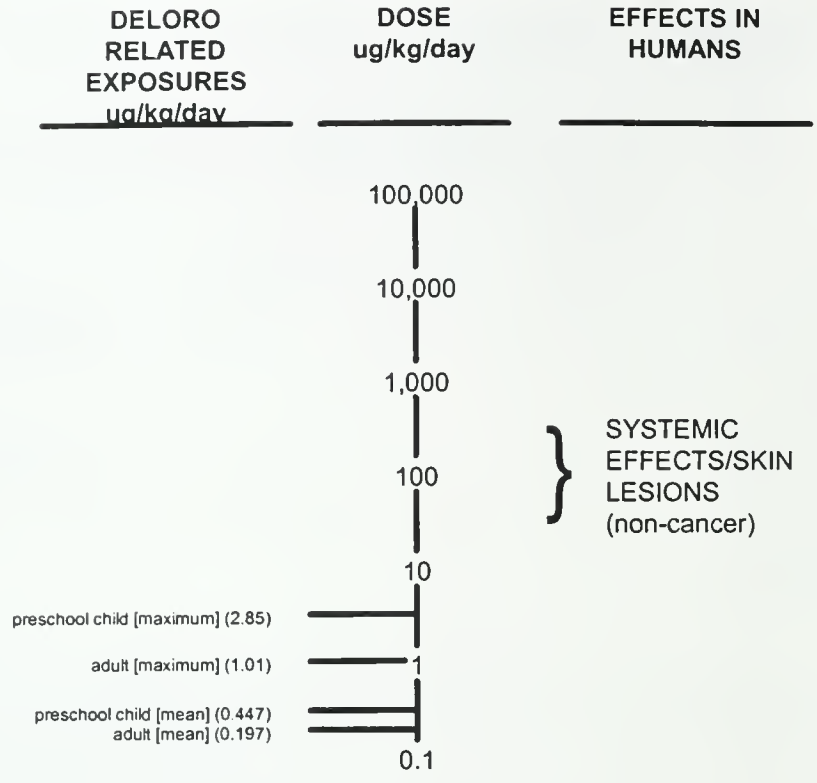
TABLE 5 Arsenic (Non-Carcinogen) Long Term Exposure Ratio Values (preschool child) for non-Home Garden Consumers

	EXPOSURE RATIO VALUES				
	DETERMINISTIC		PROBABILISTIC		
	plausible maximum	typical average	5th percentile	median	95th percentile
TYPICAL ONTARIO					
TYPICAL ONTARIO RESIDENT	6.76	1.01	0.735	2.31	5.07
DELORO ALONE					
WHOLE TOWN	3.40	0.608	0.180	0.480	1.24
ZONE 1	1.26	0.433	0.128	0.36	1.02
ZONE 2	1.54	0.474	0.148	0.382	1.04
ZONE 3	3.35	0.668	0.233	0.593	1.50
ZONE 4	4.13	0.826	0.230	0.580	1.41
DELORO INCLUDING BACKGROUND					
WHOLE TOWN	9.77	1.54	1.11	2.81	5.58
ZONE 1	7.63	1.36	1.01	2.75	5.48
ZONE 2	7.91	1.40	1.00	2.73	5.55
ZONE 3	9.72	1.60	1.23	2.97	5.88
ZONE 4	10.5	1.75	1.22	3.00	5.70

TABLE 6 Incremental Arsenic (Non-Carcinogen) Long Term Exposure Ratio Values (preschool child) for Whole Town

	EXPOSURE RATIO VALUES				
	DETERMINISTIC		PROBABILISTIC		
	plausible maximum	typical average	5th percentile	median	95th percentile
Typical Ontario resident	6.79	1.02	0.745	2.35	5.15
Deloro alone (no home garden consumption)	3.40	0.608	0.180	0.480	1.24
Deloro alone (home garden consumption included)	3.63	0.640	0.203	0.508	1.29
Deloro including home garden consumption & background contribution	10	1.57	1.15	2.87	5.63

The probabilistic assessment indicated that the lower end of the range of exposures (5th percentile) for all typical Ontario receptors except the infant were less than the toxicological criterion, while the upper end (95th percentile) exposures for all typical Ontario receptors exceeded the toxicological criterion. In the absence of consumption of home garden produce, the 95th percentile ER values for Deloro residents were slightly elevated, by about 0.2-fold, over that of typical Ontario residents (5.58 versus 5.07 for 95th percentiles for the preschool child). The toxicological criterion for the non-carcinogenic endpoints of arsenic, derived by the U.S. EPA, is based on adverse skin effects (hyperpigmentation, keratosis). Other regulatory agencies have derived criteria to be protective of the non-carcinogenic endpoints of arsenic; Health Canada, for example, has promulgated a guideline protective of induction of symptoms of chronic arsenic poisoning of 2 µg/kg bw/d, as compared to the U.S. EPA value of 0.3 µg/kg bw/d. Although the more conservative value was employed in the risk assessment, use of the Health Canada guideline in the risk assessment would have resulted in the estimation of exposures for both Deloro and Ontario residents that were at or below the toxicological criterion (with a 95th percentile of 0.84). A graphical representation of the estimated exposures of Deloro residents in comparison to the range of doses observed to cause adverse non-cancer effects in humans is provided below. The occurrence of systemic effects and/or skin lesions in human populations exposed to arsenic has been associated with exposure levels much higher than those predicted for Deloro residents.



Given the conservatism in the toxicological criterion, and given that the estimated risks to Deloro residents very marginally exceeded those for Ontario residents, it was concluded that there would be no unacceptable risks posed to Deloro residents from concentrations of arsenic within the village.

As in the assessment of arsenic on a carcinogenic basis, general food basket contributed a significant proportion of the overall risks to Deloro residents. While the major contributor to Deloro-specific risks was municipal drinking water, the concentrations in drinking water in Deloro were well below Ontario drinking water objectives for safety. Dermal contact with soils/dusts and, for small children, dust and soil ingestion were minor contributors to risk. With the consumption of home garden produce, ER values increased minimally for Deloro residents (less than 0.02-fold higher).

Cobalt

Both the mean and maximum plausible estimates of exposure for residents of Deloro (whole town, and for each zone) were less than the toxicological criterion (as indicated by ERs less than 1.0), which indicates that there would be no measurable risk of adverse health effects (polycythemia or metaplasia of the larynx). Mean exposures for typical Ontario residents, however, approached, and for the preschool child, slightly exceeded, the toxicological criterion. The maximum typical Ontario exposures were slightly in exceedence of the

toxicological criterion (up to about 3.5-fold for the preschool child). Thus, the exposure estimates for Deloro residents were less than the toxicological criterion, and risk estimates for Deloro residents were well below that for typical Ontarians, with and without the consumption of home garden produce. Therefore, based on both the comparison to predicted risks for typical Ontario residents and the comparison to the toxicological criterion, it was concluded that the exposures to cobalt associated with environmental media in Deloro would not be associated with measurable risks of adverse health effects.

Lead

Lead exposures of Deloro residents not consuming home garden produce only marginally exceeded the toxicological criterion, which was based on neurological effects in children, even at the plausible maximum. Except for the infant, mean exposure estimates for the age classes were less than the criterion (as indicated by ER values of 0.753 for preschool children), while plausible maximum values were up to 2.2-fold higher than the criterion. Similarly, mean typical Ontario exposures for all receptors were less than the toxicological criterion (ER of 0.913 for preschool children), although they were only marginally less for infants, while maximum estimated exposures ranged up to 2.55 times higher than the criterion (Table 7 and Figures 8 & 9). As can be interpreted from the ER values cited in Tables 8 and 9, without the consumption of home garden produce, maximum and mean neurotoxicity risk estimates for typical Ontario residents exceeded those for Deloro residents (by about 0.2-fold).

When potential exposures associated with consumption of home garden produce were assessed, increases in estimated exposures of Deloro residents were observed, with ERs of consumers up to about 2.5 times those of non-consumers. Mean exposure estimates exceeded the toxicological criterion only for preschool children, while maximum exposures exceeded the toxicological criterion for all age classes of Deloro residents (with ER values up to 5.86). The observed increase in exposure and risk was considered marginal, however, since exposures of home garden produce-consuming Deloro residents were greater than the toxicological criterion and typical Ontario exposures, risks associated with lead were more rigorously examined in the probabilistic assessment.

TABLE 7 Lead Long-term Exposure Ratio Values (preschool child) for Home Garden Consumers

	EXPOSURE RATIO VALUES				
	DETERMINISTIC		PROBABILISTIC		
	plausible maximum	typical average	5th percentile	median	95th percentile
TYPICAL ONTARIO					
TYPICAL ONTARIO RESIDENT	2.55	0.913	0.761	0.993	1.59
DELORO ALONE					
WHOLE TOWN	4.29	0.570	0.181	0.626	1.95
ZONE 1	3.42	0.213	0.0802	0.278	0.826
ZONE 2	1.8	0.251	0.140	0.643	2.21
ZONE 3	5.08	0.742	0.365	1.10	3.45
ZONE 4	2.48	0.454	0.196	0.498	1.27
DELORO INCLUDING BACKGROUND					
WHOLE TOWN	5.07	1.17	0.798	1.25	2.59
ZONE 1	4.19	0.814	0.692	0.909	1.49
ZONE 2	2.57	0.852	0.752	1.27	2.87
ZONE 3	5.86	1.34	0.974	1.73	4.10
ZONE 4	3.26	1.05	0.806	1.13	1.93

TABLE 8 Lead Long-term Exposure Ratio Values (preschool child) for non-Home Garden Consumers

	EXPOSURE RATIO VALUES				
	DETERMINISTIC		PROBABILISTIC		
	plausible maximum	typical average	5th percentile	median	95th percentile
TYPICAL ONTARIO					
TYPICAL ONTARIO RESIDENT	2.14	0.753	0.658	0.829	1.39
DELORO ALONE					
WHOLE TOWN	1.21	0.146	0.0428	0.16	0.545
ZONE 1	2.35	0.0605	0.0237	0.0949	0.304
ZONE 2	0.628	0.0695	0.0323	0.152	0.572
ZONE 3	1.40	0.187	0.0579	0.227	0.845
ZONE 4	0.787	0.118	0.0371	0.135	0.419
DELORO INCLUDING BACKGROUND					
WHOLE TOWN	1.99	0.746	0.646	0.789	1.23
ZONE 1	3.13	0.661	0.625	0.724	0.989
ZONE 2	1.40	0.67	0.634	0.781	1.24
ZONE 3	2.17	0.787	0.657	0.857	1.52
ZONE 4	1.56	0.718	0.637	0.761	1.10

TABLE 9 Incremental Lead Long-term Exposure Ratio Values (preschool child) for Whole Town

	EXPOSURE RATIO VALUES				
	DETERMINISTIC		PROBABILISTIC		
	plausible maximum	typical average	5th percentile	median	95th percentile
Typical Ontario resident	2.14	0.753	0.658	0.829	1.39
Deloro alone (no home garden consumption)	1.21	0.146	0.0428	0.16	0.545
Deloro alone (home garden consumption included)	4.29	0.570	0.181	0.626	1.95
Deloro including home garden consumption & background contribution	5.07	1.17	0.798	1.25	2.59

In the probabilistic analysis (Figure 10), estimated exposures for typical Ontario infants, preschool children and children ranged from below the toxicological criterion for the 5th percentile results (ER of 0.761 for preschool children) to slightly in exceedence of the limit for the 95th percentile (ER of 1.59) (see Table 7). 5th and 95th percentile exposures for typical Ontario adolescents and adults were both less than the toxicological criterion. For Deloro residents, in the absence of exposure to lead through the consumption of home garden produce, the 5th and 95th percentile ERs were slightly less than those reported for typical Ontario exposures for all receptors except the infant (ERs of 0.657 and 1.52, respectively, for preschool children). While 5th percentile ER values for the infant resident of Deloro village were less than typical Ontario residents, the 95th percentile values for the infant for the whole town and, Zones 2 and 3 were marginally in exceedence of typical Ontario 95th percentiles. These increments were slight, and were observed only for the infant, for whom a major contributor, soil/dust ingestion, was likely overestimated. Therefore, in the absence of consumption of home garden produce, exposures to lead in environmental media within Deloro were not considered to increase overall risks of residents, and would not be associated with a measurable increase in risks of neurological effects.

The major contributors to the risks to typical Ontario residents associated with lead were the general food basket and, to a lesser extent, drinking water. The contributors to overall risks for residents of Deloro indicated that the significance of contribution due to various exposure pathways was greatly dependent on receptor characteristics. Reviewing the predicted exposures in the absence of consumption of home garden produce, soil/dust ingestion contributed 45 to 60% of maximum risks for the infant and preschool child, and 20 to 25% of the mean risks, respectively. Again without home garden consumption, these pathways contributed 16 and about 2% of the maximum and mean overall risks for adults. Contributions to mean exposure via the general food basket ranged from about 71% for infants and preschool children to 90% for adults, while general food basket contributed about

25 and 50% to maximum exposures, for children and adults, respectively. Drinking water consumption provided a significant pathway of exposure (without home garden) as well, with consumption of Deloro municipal water contributing 10 to 20% of the maximum, and 1 to 2% of the mean risks for all receptors; similar but lower contributions were made by consumption of water from Ontario sources. The greater contribution to exposure to lead in drinking water from Deloro was due to the greater daily consumption within Deloro, as concentrations in Deloro municipal water were one fourth to one seventh of the values report for Ontario drinking water. As shown in Figure 11, the consumption of home garden produce contributed about 60% of the overall maximum risks, respectively, to Deloro residents. Other pathways correspondingly decreased in proportional contribution, with general food basket about 15%, soil/dust pathways about 10%, and drinking water about 5% of the overall risks.

The maximum probabilistic ER value for lead of Deloro residents consuming home garden produce was 4.10. Although this is indicative of exposures exceeding the criterion based on neurological effects, an exceedence of this magnitude was not considered to be of concern, given the conservatism inherent in this risk assessment. The toxicological criterion is based on the lowest effective blood lead level reported in epidemiological studies of the effects of lead in human infants, who are considered to be the most sensitive receptors, based on both their susceptibility to neurodevelopmental effects as well as their higher gastrointestinal absorption of lead. In addition, the estimation of risks specifically to consumers of home garden produce was considered to be conservative for several reasons. These include the use of the entire range of concentrations throughout Deloro in the estimation of exposure included concentrations, not just those in back yards and gardens. Because home garden produce is more likely grown in these areas, which had lower concentrations, actual exposures and risks are expected to be lower. Based on this overestimation, and on the minimal increase in risks, the exposures to lead from consumption of home garden produce is not expected to measurably increase risks to Deloro residents.

To put the surface soil concentrations of lead in Deloro into perspective, they were compared to concentrations found elsewhere in Ontario and were found to be in general agreement with the reported concentrations in urban soils (average 123 mg/kg, maximum 845 mg/kg for urban Ontario soils, as compared to 121 and 655 mg/kg for the average and maximum in Deloro soils). The importance of exposure to lead via direct soil pathways to overall risks of typical Ontario residents was re-examined based on the acceptable blood lead level (PbB) of 10 µg/dL, and in the context of several models describing the relationship between PbB and exposure via all relevant exposure pathways. Several agencies, including the Centers for Disease Control and the U.S. EPA, have indicated a necessity for soil concentrations greater than 500 to 1000 mg/kg before blood lead levels in children would be greater than typical background levels. In their Scientific Criteria Document (1994) the OMOE investigated several models of environmental exposure to lead. These included the Integrated Uptake/Biokinetic Model (IU/BK), which calculates PbB based on environmental media concentrations, and the Society for Environmental Geochemistry and Health Model (SEGH), which relates soil concentrations to PbB. The results of both models, as cited by the OMOE, indicate that, in agreement with the CDC and U.S. EPA findings, soil concentrations would

have to exceed 600 and 855 mg/kg, based on the IU/BK and SEGH models respectively, before blood lead levels of children would exceed the acceptable PbB of 10 µg/dL. This further supports the conclusion of the current assessment that concentrations of lead in Deloro soils would have no measurable impact on overall exposure and risk of Deloro residents.

Nickel

The mean and maximum exposures determined for nickel, with and without consumption of home garden produce, were elevated above the toxicological criterion for exposures associated with typical Ontario, whole town and each of the zones. The ERs for overall exposure of Deloro residents were much less than those for exposures of a typical Ontario resident, and, indeed, the majority of risks predicted for Deloro residents were derived from exposures not associated specifically with the town (*i.e.*, the general food basket). Given that mean and maximum typical Ontario risks exceeded the risks predicted for Deloro residents, and given that the majority of the risk indicated for Deloro residents was contributed by general food basket common to all Ontario residents, concentrations of nickel in Deloro environmental media were not considered to pose an increased risk of adverse health effects, in comparison to typical Ontario.

Silver

With and without the consumption of home garden produce, mean and maximum exposures for the whole town and each of the zones were less than the toxicological criterion (based on induction of argyria) for all receptors except the infant and the preschool child (as indicated by ERs less than 1.0). For the infant, both mean and maximum exposures slightly exceeded the toxicological criterion, while only the maximum exposure for the preschool child exceeded the toxicological criterion. Argyria risk estimates for Deloro residents were slightly greater than those calculated for exposures of a typical resident of Ontario. Given that the toxicological criterion for silver is based on the induction of argyria, a strictly cosmetic alteration of colouring which is not associated with any type of tissue damage or actual adverse health effect, that contributions to risk not associated with Deloro, based mainly on a highly conservative estimate of intake via general food basket, especially for infants and children, comprised such a high proportion of the total risk, and that the exceedence of the toxicological criterion was marginal, it was concluded that concentrations of silver in environmental media in the village of Deloro would not result in a measurable increase in risk of adverse health effects.

Relevance of Exposures via Soil and Dust

The significance of contamination in indoor dust and outdoor soils and dusts within Deloro to the exposure and risk of its residents varied for each of the chemicals of concern. Direct exposure pathways for soil and dusts include accidental ingestion of soils or dust, inhalation of airborne particles, and dermal contact with soils. An indirect pathway of exposure to

contaminants in soils, consumption of fruits and vegetables grown in home gardens, is discussed separately, below.

For cobalt, nickel and silver, the ingestion, inhalation and dermal exposure via indoor and outdoor soil/dust contributed relatively minor proportions of overall risks of Deloro residents who also consumed home garden produce.

For lead, direct exposure pathways for soils and dusts contributed a higher proportion to overall risks of Deloro residents (11 to 18% for preschool children), however, overall exposures of Deloro residents, in the absence of home garden consumption, were less than that of Ontario residents, thus contributions of direct soil and dust exposure pathways to exposure would not measurably increase risk to Deloro residents. Therefore, it was concluded that since soils in Deloro do not measurably increase risk of adverse health effects, no remedial activity is required.

The deterministic analysis indicated that exposure to arsenic via direct pathways comprised a significant proportion of overall risk for Deloro residents. Children experienced relatively higher exposures via soil ingestion (contributing about 10% to overall deterministic risks) than did adults (contributing 2%). Contribution to overall risk by exposure via dermal contact was similar in both children and adults (5 to 25% and 10 to 20%, respectively, for mean and maximum deterministic estimates). The importance of examining specific environmental media with respect to impacts on the overall risks for Deloro residents lies in the utilization of such information to guide risk management decisions. Since direct exposure pathways for soil/dust was identified in the deterministic analysis as a contributor to overall risk for arsenic, for both children and adults residing in Deloro, the importance of these pathways to risk estimation in the more rigorous probabilistic analysis was also evaluated. This allowed the incorporation of the more realistic modelling of the probabilistic analysis in development of risk management recommendations for the two metals considered to be of potential concern. In theoretical probabilistic modelling, it was determined that cessation of direct exposure to soils and dusts (*i.e.*, ingestion, inhalation or dermal contact with indoor and outdoor soils/dust), would result in only a 2 to 4% reduction (for 95^{th} and 5^{th} percentiles, respectively) in the overall risks for the composite receptor. Therefore, it can be concluded that even if concentrations of arsenic in soils and dusts were reduced to equal typical Ontario concentrations, there would be no measurable reduction of exposure to arsenic, based on direct contact pathways.

In conclusion, the results of the probabilistic analysis indicated that the exposures to Deloro residents to arsenic and lead in soils and dusts via direct contact pathways (ingestion, inhalation, and dermal contact) were not sufficient to require remediation of soils and dusts. The impact of such remediation on overall risks would be negligible, and would not result in any measurable decrease in predicted risks.

Relevance of Consumption of Home Garden Produce

The contribution of the consumption of home garden produce grown in Deloro to estimates of overall risks varied considerably with the chemical under examination. While the deterministic analysis indicated that contribution of home garden produce to overall risks associated with cobalt was less than 2%, risks from the consumption of home garden produce contributed approximately 60 to 70% of the maximum and 30 to 40% of the mean overall risks for lead. Intermediate contributions of home garden produce consumption are indicated for the other metals, such as arsenic, for which home garden contributed about 10% of the predicted deterministic risks. For lead, vegetables (especially root vegetables) contributed about 80% of the home garden exposure.

Given that exposures through the consumption of home garden produce were negligible for most of the metals, and given the marginal increase in overall risks for lead for Deloro residents in comparison to typical Ontario residents, it was concluded that the use of the home garden did not measurably increase risks to Deloro residents, and did not require remediation.

Relevance of Exposures via Trespassing on the Mine Site

In general, only for maximum risk estimates for arsenic (carcinogenic and non-carcinogenic endpoint) were there significant increases in the CRL/ER values following addition of the trespasser scenario. Contributions of trespasser exposures to mean predicted risks for arsenic were minimal, and the contributions of the trespasser scenario to mean and maximum risks for cobalt, lead, nickel, and silver were negligible. It was concluded that the results for the trespasser scenario likely overestimated risks to Deloro residents by a significant a degree, especially for arsenic. For example, there are concerns about the validity of the use of the maximum concentrations of arsenic reported for the mine site, given the unlikelihood that a resident hiking on the mine site would spend any prolonged period of time in contact with these areas of extreme concentrations. Additionally, the trespasser scenario considered direct contact soil related exposure pathways similar to those considered for the town, while it is expected that people will only spend time walking on the mine site. It was concluded that the trespassing on the mine property may contribute significantly to the overall risks of Deloro residents, and therefore, mitigation of this exposure (*e.g.*, through limited access) will be considered in development of the remediation plan for the site.

Urinary Arsenic Evaluation

A non-parametric statistical test revealed there were no significant differences of total and speciated urinary arsenic levels between residents in Deloro Village (on a whole town basis, as well as for each of the four zones) and residents in Havelock. The measured urinary arsenic concentrations were also compared to concentrations reported in the published literature. The mean urinary arsenic concentrations of residents from both Deloro and Havelock fall in the range of typical Ontario areas, and are much less than the means reported

for persons exposed to point sources of arsenic (such as mining/smelting, occupational, *etc.*) (see Figure 12).

In order to validate the exposure and urinary arsenic modelling, the measured values were also compared to predicted concentrations. The results of the urinary arsenic model were generally in good agreement with the measured concentrations in Deloro and Havelock. The slight overestimation of urinary arsenic concentrations indicates the exposure assessment modelling was based on conservative values and assumptions, and that therefore the risk characterization was also conservative, and the predicted risks were overestimated.

Uncertainty and Sensitivity Analysis

As part of the current assessment, a sensitivity analysis was conducted in order to identify the variables to which the risk characterization was most sensitive. It was observed that the variables to which the assessment was sensitive were model parameters which were considered to be realistic and conservative in nature. As such, there was confidence that the risk characterization results were accordingly realistic and conservative.

Several uncertainties were identified throughout the course of the assessment, in the following general areas:

- Environmental media concentrations (*e.g.*, regarding concentrations less than detection in municipal well water, extrapolation of vegetable biotransfer factors from garden test plots to entire village and validity of the extrapolation to fruits, extrapolation of indoor air concentrations from outdoor air, validity of exposure via general food basket common to all Ontarians).

- Biomonitoring analytical results (*i.e.*, a large number of speciated urinary arsenic samples were less than the detection limit, which introduces some uncertainty only into the validation of the urinary arsenic model).

- Receptor physiological and behavioural parameters (*e.g.*, the amount of time a receptor may spend on the abandoned mine site; soil ingestion by infants; intake of home garden produce; urinary volumes).

- Toxicological criteria derivations (*e.g.*, use of most conservative toxicological criterion, humans were assumed to be the most sensitive species, conservatism was introduced by applying large uncertainty factors to limits for chemicals with threshold-type dose-responses). In the case of arsenic, there are concerns that the oral cancer potency for arsenic based on exposures of Taiwanese populations to arsenic in drinking water, may significantly overestimate skin cancer risks at lower exposure levels more representative of those experienced by the general North American population.

Given the above, this risk assessment may overestimate actual risks by a considerable degree, but will not underestimate potential health risks. However, due to the relatively large database of site specific information and the comprehensive nature of the probabilistic component of this assessment, this overestimation is not expected to be unduly unrealistic.

Risk Management: Exposure And/or Risk Mitigation

CANTOX ENVIRONMENTAL makes the following recommendations:

With Regard to Predicted Risks Associated with Exposure to Arsenic:

The current risk assessment indicated that exposures associated with direct soil and dust pathways did not contribute significantly to overall risks of Deloro residents. Thus remediation of the mine site would not be expected to measurably impact the estimated risks; however, such remediation would prevent future contamination of Deloro by arsenic, and would thus ensure that conditions in Deloro improved in future. If deemed necessary, the following options would mitigate future contamination of environmental media in Deloro by preventing mobilization from the site:

- Stabilization of tailings,
- Capping, or covering the contaminated soil or tailings with clean topsoil,
- Excavation of heavily contaminated soils,
- Solidification/stabilization limits contaminant mobility, although this is considered to need further research before it could be considered a candidate technology for the mitigation of arsenic exposure.

The results of the urinary arsenic evaluation were sufficient to allow the conclusion that this "snap-shot" of exposures experienced by Deloro residents in September are within the range of concentrations reported for Havelock, and within the range of individuals not exposed to any point sources of arsenic.

With Regard to Exposures to Arsenic Associated with Trespassing on the Former Mine Site:

For arsenic, the risk characterization indicated that trespassing on the former mine site was a potentially significant contributor to risk for Deloro residents. Given this, and given the inherent uncertainties in the estimation of the exposures and risks via this scenario (regarding time activity patterns, types of exposure, and distribution of concentrations on the mine site), some mitigation of mine site exposures should be considered. This may involve restriction access to the areas of the site with extremely high concentrations, or in some way preventing exposure to these extreme concentrations (e.g., capping, stabilization, excavation).

Conclusions

Everyone in Ontario is exposed to arsenic, lead and other metals and has a certain level of risk. This is because trace elements like arsenic are present in our environments wherever we live. When people living anywhere are exposed to arsenic, the greatest potential health risk is the development of skin cancer and, to a lesser degree, lung cancer. Studies elsewhere have also shown that high arsenic exposures are associated with internal cancers such as bladder cancer.

Exposure and risk estimates for Deloro residents were compared against the exposure and risk estimates for typical Ontario adults and children and it was found that overall exposures to arsenic were only marginally greater for Deloro.

- Estimated arsenic exposures are not measurably higher than those of typical Ontario residents.

- Overall exposures and risks for arsenic were only slightly greater when compared to estimates for the typical Ontario resident. For example, predicted maximum cancer risk for arsenic in Deloro from all pathways totaled was about 0.2 times higher than the mean risk for typical Ontario exposure (1.17 per 1000 for Deloro versus 0.963 per 1000 for Ontario). Most importantly the percent contribution of exposure or dose from soil and dusts (dermal, ingestion and inhalation) was small when compared to arsenic in the normal daily diet. The presence of arsenic in the Ontario diet is due to its natural occurrence as a trace element in the earth and its uptake into crops. There are also various forms of arsenic in food which are considered non-toxic or less toxic than other forms.

- Predicted cancer and non-cancer risk levels were only slightly higher for Deloro residents than for a person living elsewhere in Ontario. For example, it was estimated that roughly 80% of lifetime risks from exposure to arsenic in Deloro is from the normal Ontario food basket as compared to roughly 4% for soil and indoor dust combined. The relative contribution of specific pathways to total lifetime risk (e.g. backyard vegetables, diet, soil) is shown in Figures 5, 6 &7. The combined risk from soil, indoor dust and home garden produce is 1/10th that of the regular Ontario food basket. Furthermore, the levels of risk for each of the soil and indoor dust, and backyard vegetable pathways were found to be in the range which is considered negligible.

- If all soils in Deloro were replaced with background soils, overall risks from arsenic would be reduced by only 2-4%.

- Deloro residents would not experience risks from exposure to lead that were significantly greater than typical Ontario residents. No adverse health effects would be expected to occur at the levels of lead found in the village, as these levels were not unusually high.

- Levels of cobalt and silver in the village of Deloro are not high enough to result in any measurable health risk. Risks from exposure to nickel in Deloro were comparable to typical Ontario residents.

- The levels of contaminants in drinking water were all well below objectives for safety.

Figure 1 Exposure Pathways for Human Health Risk Assessment

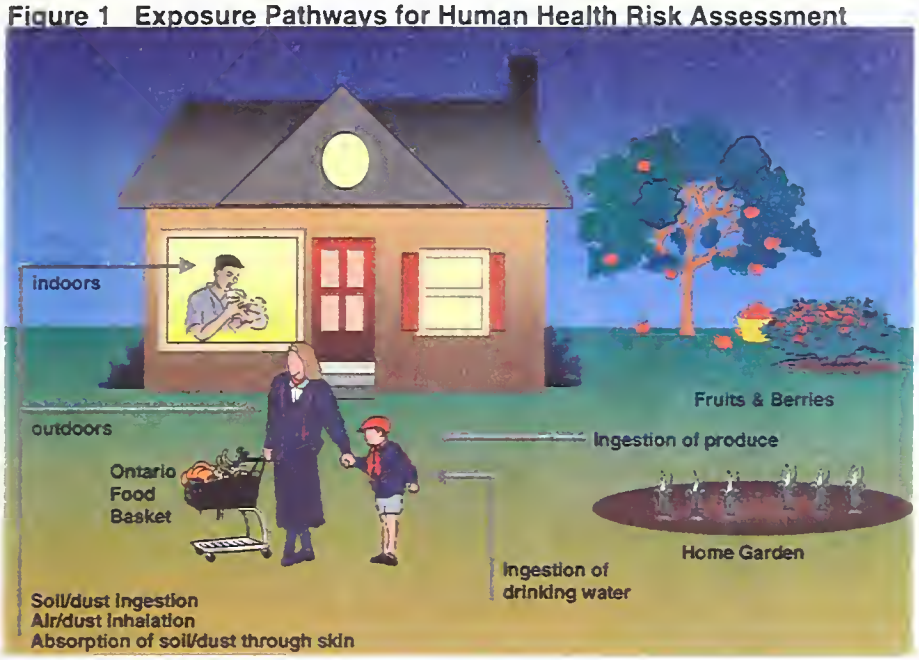


Figure 2
Estimated Lifetime Cancer Risk Levels (Deterministic)
Arsenic (all cancers)-home garden consumers

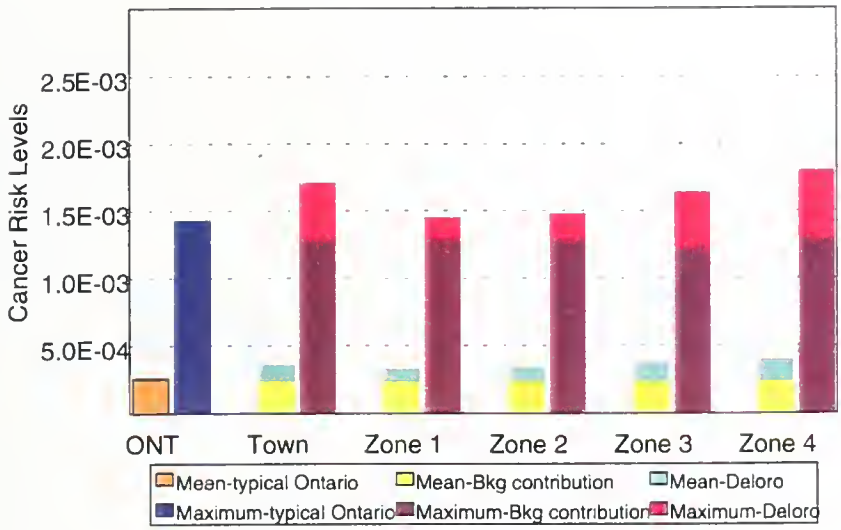


Figure 3
Incremental Estimated Lifetime Cancer Risk Levels (Determinist
Arsenic (all cancers)-WHOLE TOWN

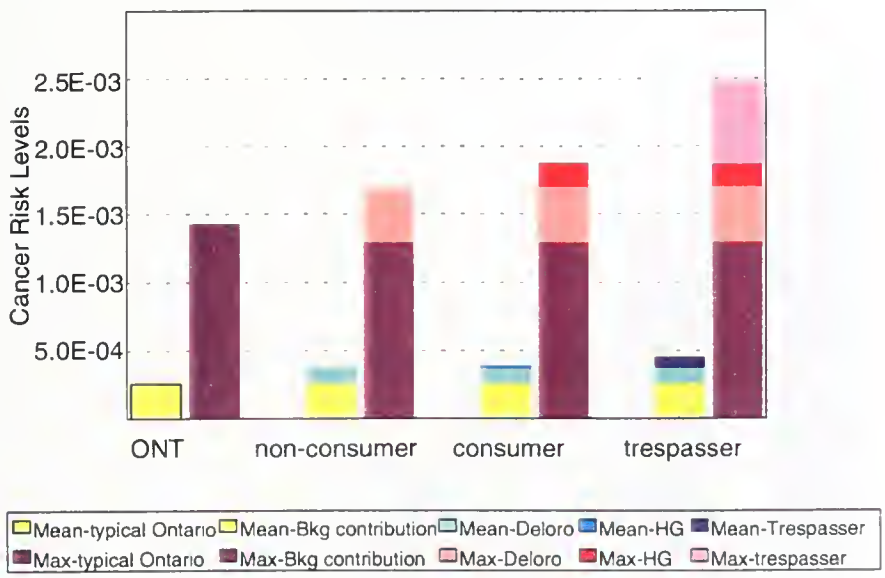


Figure 4
Incremental Lifetime Cancer Risk Levels (Probabilistic)
Arsenic (all cancers)-WHOLE TOWN

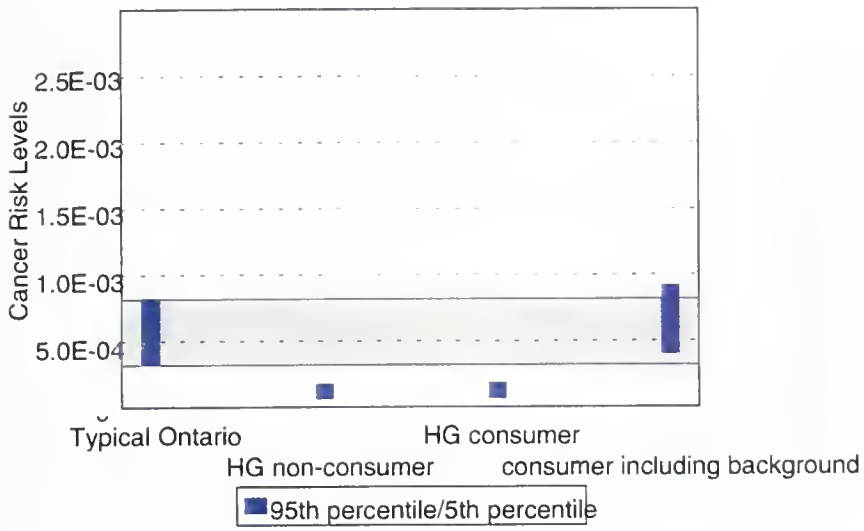


Figure 5 Contribution of Various Pathways to Preschool Child Receptor Exposure to Arsenic (Probabilistic Mean)

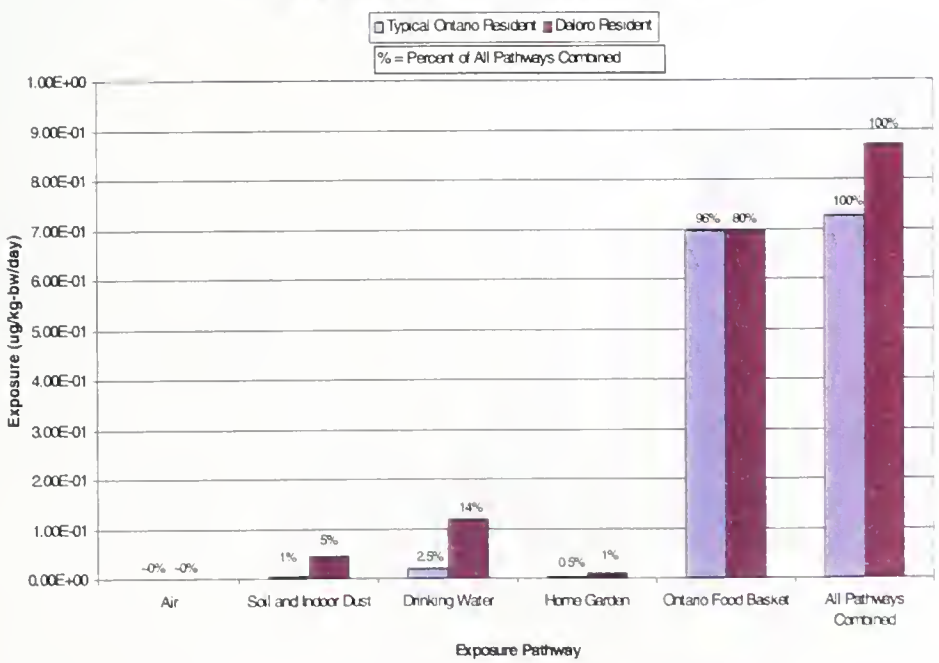


Figure 6 Contribution of Various Pathways to Adult Receptor Exposure to Arsenic (Probabilistic Mean)

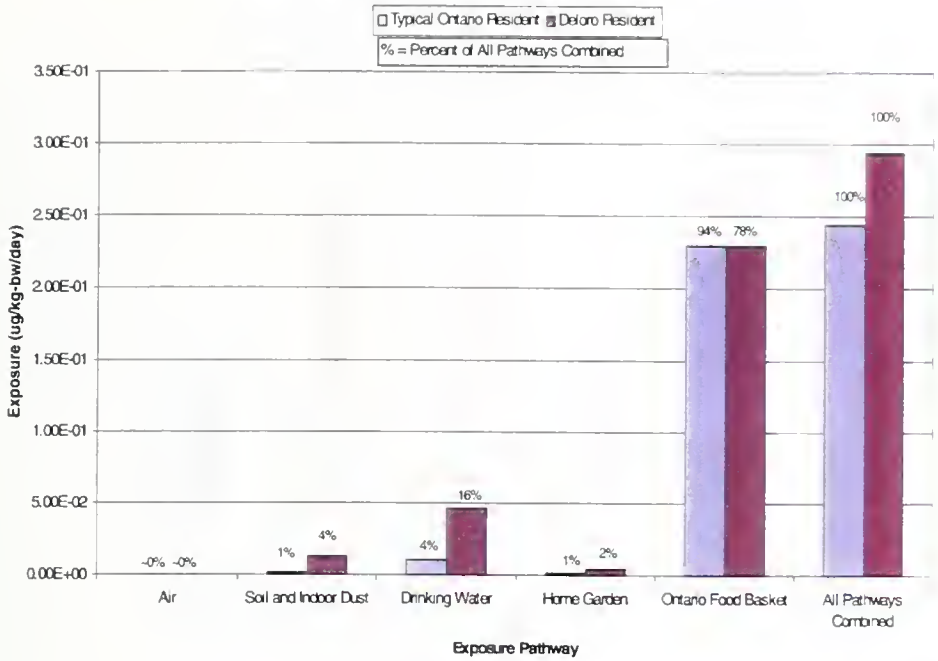


Figure 7 Contribution of Various Exposure Pathways to Lifetime Risk from Exposure to Arsenic (Probabilistic Mean)

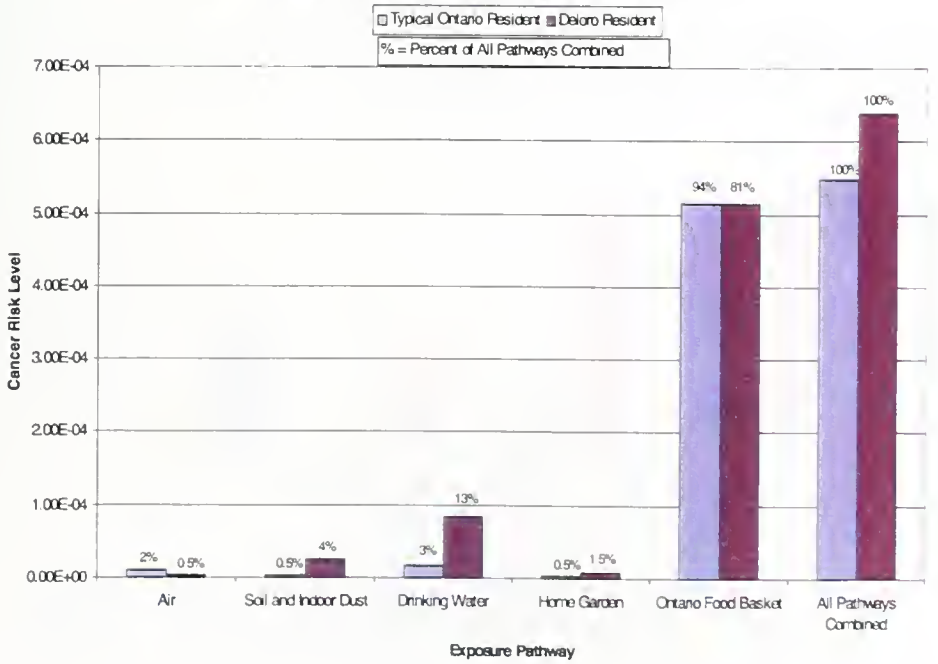


Figure 8
Long-term Exposure Ratios (Deterministic)
Lead-home garden consumers

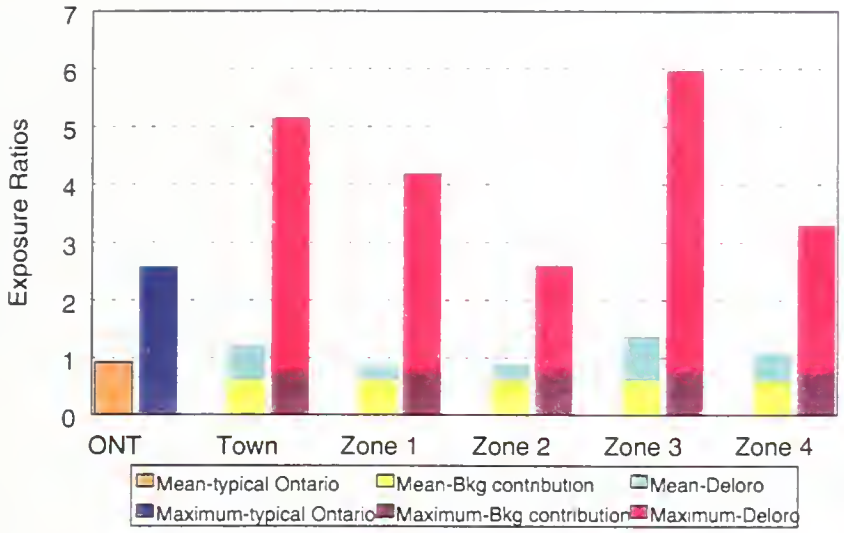


Figure 9
Incremental Long-term Exposure Ratios (Deterministic)
Lead-WHOLE TOWN

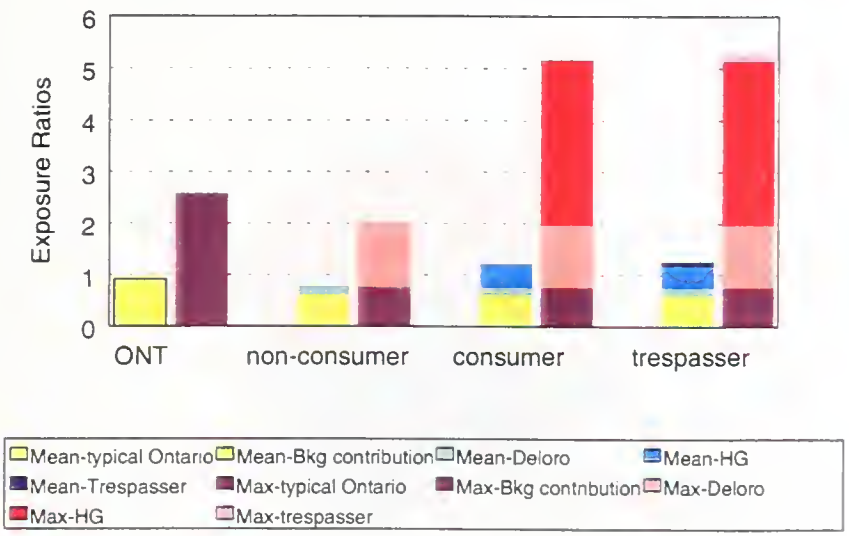


Figure 10
Incremental Long-term Exposure Ratios (Probabilistic)
Lead-WHOLE TOWN

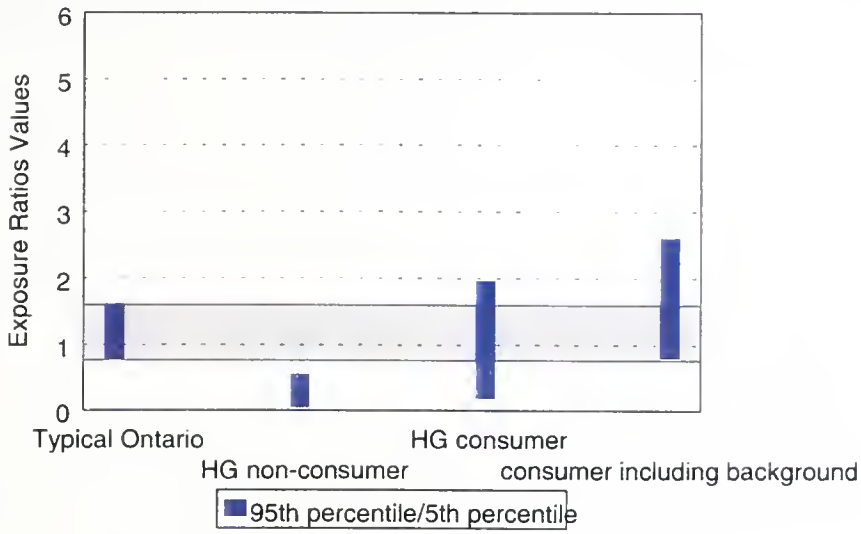
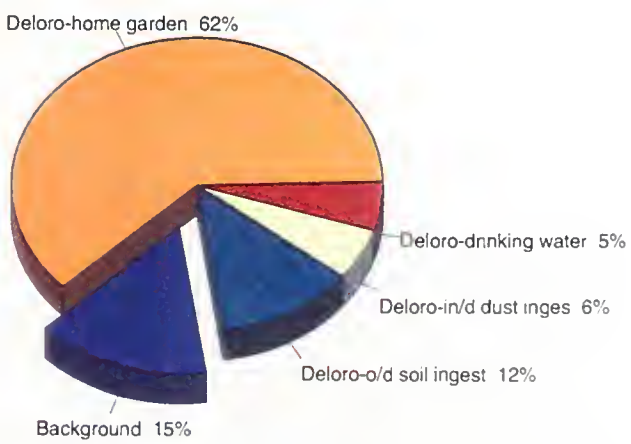
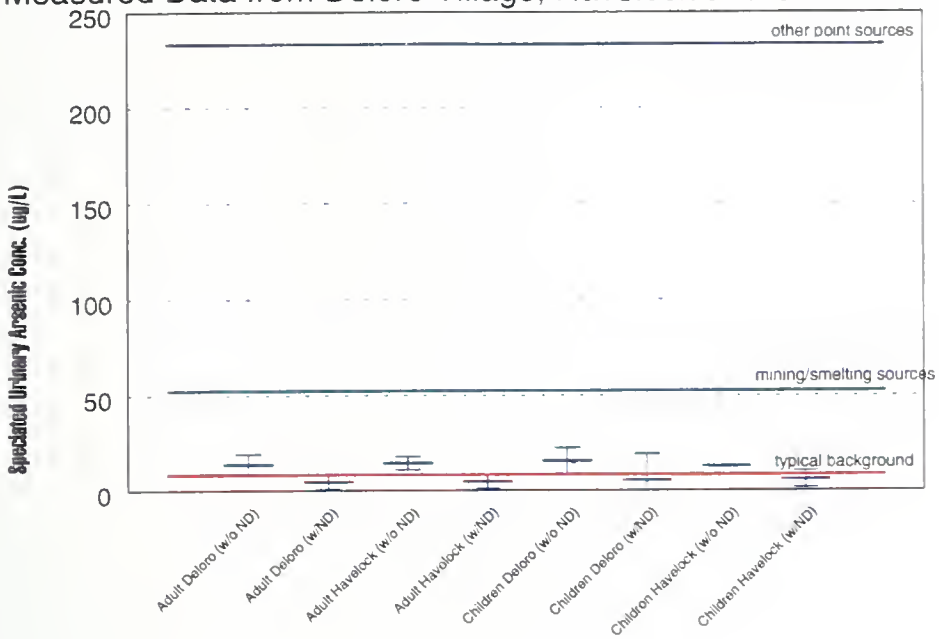


Figure 11
Exposure Pathways Analysis (% of Risk) - Lead
[maximum preschool child home garden consumer]



pathways contributing to greater than 1% of the overall risk (ER) are included

Figure 12
Speciated Urinary Arsenic Concentrations
Measured Data from Deloro Village, Havelock and Other Areas



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CANTOX ENVIRONMENTAL

DELORO VILLAGE
EXPOSURE ASSESSMENT AND HEALTH RISK CHARACTERIZATION FOR ARSENIC AND OTHER METALS

PART 1 - INTRODUCTION

December, 1999

PART 1
INTRODUCTION

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PART 1
INTRODUCTION

1.0 INTRODUCTION

The Village of Deloro, located on the Moira River in southeastern Ontario, approximately 40 km north of Belleville, is the focus of an extensive risk assessment and remediation effort by the Ontario Ministry of the Environment (OMOE). The village is located along the property line of a former mine and refinery, and is home to a population of 140 people (40 of which are children) in 65 residences. Contamination of the former Deloro mine site and the vicinity is the result of a century of refining various ores from mines in the vicinity as well as from other mines in Northern Ontario. In addition, radioactive slag was imported to Deloro from Eldorado Nuclear. The mine site and refinery were abandoned in the 1960s. The current effort is aimed at quantifying and mitigating exposures and risks to the residents of Deloro which are associated with the contamination of the former mine site by heavy metals and radiological agents and the subsequent emission of contaminants from the site via liberation of dusts, volatilization, and/or leaching into the Moira River watershed.

The OMOE has conducted a screening level risk assessment on the contaminated soils of the village of Deloro, and have identified several heavy metals (arsenic, cobalt, lead, nickel, and silver) as well as radiological agents as being of potential health concern to residents.

Under the leadership of OMOE and CH2M Gore & Storrie Limited (CGS), a multidisciplinary approach has been adopted to characterize the media-specific concentrations of chemicals of concern in Deloro Village, to assess the exposures experienced by Deloro residents (both through exposure modelling and through biological monitoring), and to determine potential risks to the residents, based on these parameters. CANTOX ENVIRONMENTAL INC. has been requested to conduct an exposure assessment and health risk characterization for the residents of Deloro, Ontario, based on concentrations of arsenic and the other metals of potential concern in media (air, drinking water, soil, food) throughout the village. For the purposes of this assessment, the former mine was considered to be the "site", and the current assessment was conducted for off-site exposures experienced by individuals dwelling in the vicinity of the former mine, but without routine access to the mine site; although occasion visits onto the site were considered.

The exposure assessment and risk characterization was conducted in compliance with the risk assessment procedures endorsed by regulatory agencies including the Ontario Ministry of the Environment (OMOE, 1997), Health Canada, and the United States Environmental Protection Agency (U.S. EPA, 1989). In addition to ongoing communications with OMOE personnel specifically in regard to this assessment, past experience with the Standards Development Branch of the OMOE was considered during the methods development stage of this assessment, in order to ensure compliance with all regulations governing the use of risk assessment in Ontario.

The objectives of this assessment were as follows:

(i) to review the exposures and/or risks posed to the public in the vicinity of other mining or smelting operations in North America;

(ii) to review the sources and levels of exposure of chemicals of concern to typical Ontarians, including home grown and market basket foods, soils, drinking water, and air;

(iii) to determine if the concentrations of arsenic and the other metals of concern in various media in Deloro would pose a risk of adverse health effects for adults and children dwelling in the village, and to compare results to exposures in other mining/smelter areas as well as exposures of typical Ontario residents;

(iv) to compare the results of exposure assessment to those of biological monitoring efforts (specifically urinary arsenic determinations); and,

(v) review various options of exposure and risk mitigation and make estimates of possible risk reductions.

The following report details the exposure and risk assessment for the residents of the village of Deloro. Part 2 of this report provides a general methodology for exposure, toxicological and risk assessment as well as uncertainty and sensitivity analysis. Part 3 contains a comprehensive review of arsenic exposures experienced near mining/smelting operations and by typical Ontario residents. Part 4 presents comprehensive toxicological reviews for each of the chemicals of concern. Part 5 provides the specific methodologies, results and discussion of the risk assessment and the urinary arsenic modelling efforts. Part 6 presents overall conclusions of this report, together with recommendations regarding future activities. Receptor parameters, environmental concentrations and detailed results are provided in Appendices A, B, and C, respectively. Appendix D provides the expert peer review comments and CANTOX ENVIRONMENTAL's response to the peer review.

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CANTOX ENVIRONMENTAL

DELORO VILLAGE
EXPOSURE ASSESSMENT AND HEALTH RISK CHARACTERIZATION FOR ARSENIC AND OTHER METALS

PART 2 - GENERAL METHODOLOGY

December, 1999

PART 2
GENERAL METHODOLOGY

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PART 2
GENERAL METHODOLOGY

1.0 INTRODUCTION

For the current screening level assessment, a phased approach was followed. The five phases of the risk assessment are as follows: Phase I - Problem Formulation; Phase II - Exposure Assessment; Phase III - Hazard Assessment; Phase IV - Risk Characterization and Phase V - Risk Management.

In the characterization of the exposures and risks associated with a contaminated site, two analytical techniques are routinely used: deterministic and probabilistic analyses. These are discussed in greater detail in Section 3.0. In a fully deterministic analysis, single values, or point estimates, are used for parameters describing exposure and toxicity. Because these point estimates are selected to maximize exposure and risk, the deterministic analysis can be considered to be a "worst-case" assessment. In probabilistic (or stochastic) analysis, probability distributions are assigned to the parameters used in the assessment (*i.e.*, exposure or risk parameters) and risk estimates are expressed as cumulative probability density functions. For the current assessment, deterministic analyses are used initially, to characterize the plausible maximum ("worst-case") and typical mean exposures and risks. In cases where the potential for measurable risks are indicated by comparison to relevant toxicological criteria and to risks of typical Ontario residents, it is concluded that a more rigorous and realistic evaluation of risks should be conducted through probabilistic analysis. The various uncertainties associated with each phase of the risk assessment are examined in order to ensure that the risk characterization would be both conservative and realistic.

The computer model used to conduct the risk assessment utilized the Microsoft® Excel spreadsheet environment, under Microsoft® Windows 95.

2.0 GENERAL METHODOLOGY

2.1 Problem Formulation

Problem formulation acts as an information-gathering and interpretation stage, which is conducted to plan and focus the approach of the risk assessment on critical areas of concern for the site being evaluated. The key tasks requiring evaluation within the problem formulation phase include the following: i) site characterization, which consists of a review of available site data to identify factors affecting the availability of contaminants to potential receptors, such as location and medium of contamination and the effects of local hydrogeology on movement in the environment; ii) chemical characterization, which involves the identification of the primary chemicals of concern based on site monitoring; iii) receptor characterization to identify "receptors of concern", which include those with the greatest probability of exposure to chemicals from the site and those that have the greatest sensitivity to these chemicals; and, iv) the identification of exposure pathways, which takes into account chemical-specific parameters, such as solubility and volatility, characteristics of the site, such as physical geography, geology and hydrogeology, as well as the physiology and behaviour of the receptors.

2.2 Exposure Assessment

The assessment of potential occurrences of adverse effects from chemicals is based on the dose-response concept that is fundamental to the responses of biological systems to chemicals (Filov *et al.*, 1979; Amdur *et al.*, 1991). That is, the response of a receptor to chemical exposure will increase in proportion to the chemical concentration in critical target tissues where adverse effects may occur. Since it is not usually practical to measure concentrations of chemicals at the actual site where the adverse response occurs within tissues and cells, these concentrations are estimated based on either the dose of the chemical that actually enters a receptor or, more commonly, by the concentrations in various environmental media that act as pathways for exposure. The degree of exposure of receptors to chemicals from the environment therefore depends on the interactions of a number of parameters, including:

- The concentrations of chemicals in various environmental media (*i.e.*, soil, dusts, indoor and outdoor air, home garden produce, drinking water) as determined by the magnitude of point sources as well as background or ambient concentrations (that might be found in any typical Ontario region).

- The characteristics of the chemicals of concern which affect environmental fate and persistence (*e.g.*, physical-chemical properties, such as water solubility, volatility, tendency to bind to particles).

- The impact of site-specific characteristics, such as geology, geography and hydrogeology, on chemical behaviour, and their impact on relevance of various

exposure pathways (ingestion of water or soil, inhalation of soils, dust, air, dermal contact).

- The physiological and behavioural characteristics of the receptors that determine the actual exposures through interactions of the receptors with the various pathways (*e.g.*, respiration rate, soils/dusts intake, time spent at various activities and in different environmental areas).

- The various physical, chemical and biological factors that determine the ability of the organism to take the chemicals into the body from various exposure pathways (*e.g.*, bioavailability of the chemicals from particles, soil, air). The bioavailability of the chemical defines that portion of the exposure to a chemical (*e.g.*, the quantity inhaled or ingested) that enters the blood stream and is assumed to be available to produce toxic effects in target tissues. Bioavailability is dependent on the chemical species, the environmental media through which exposure occurs, as well as the animal species and target tissues with which the chemical interacts.

2.2.1 Consideration of Exposures Not Associated with the Site

The chemicals considered in the risk assessment may be naturally present within our environment, or have anthropogenic sources independent of their presence on or near the site under consideration. As a result, an additional exposure/risk assessment should be conducted, in order to evaluate the degree of exposure of the receptors to the selected chemicals without contribution from the site under consideration. Such an assessment would yield an indication of the exposures experienced by a typical Ontario resident, based on ambient or background concentrations in water, air, soil, dust, and food. This can then be used to account for exposures of the receptors from background or "typical Ontario" sources in addition to the site under consideration, to give a total exposure from all sources. These values are used as benchmarks of comparison, in determining the significance of the exposures from the site, in comparison to typical background exposures. Such comparisons may be useful in putting exposures into perspective (*e.g.*, if typical Ontario exposures greatly exceed site-related exposures, less concern may be accorded the site), and in guiding risk management recommendations.

2.2.2 Estimation of Exposure

The primary objective of the exposure assessment was to predict, using a series of conservative assumptions, the rate of exposure (*i.e.*, the quantity of chemical and the rate at which that quantity is received, expressed in µg/kg body weight/day) of the identified receptors to the chemicals of concern *via* the various exposure scenarios and pathways identified in the problem formulation.

The calculations used in estimation of exposures, based on the principles discussed above, are presented for each of the major pathways of exposure below:

Outdoor Dust Inhalation:

ODI = [(TSOW x OACW) + TSOS x OACS)] x AI x IB / BW

where:

ODI	=	Outdoor dust inhalation exposure (µg/kg body weight/d)
TSOW	=	Fraction of time spent outdoors at assessed location - Winter (unitless)
TSOS	=	Fraction of time spent outdoors at assessed location - Summer (unitless)
OACW	=	Outdoor air chemical concentration - Winter (µg/m^3)
OACS	=	Outdoor air chemical concentration - Summer (µg/m^3)
AI	=	Amount of air inhaled (m^3/d)
IB	=	Inhalation bioavailability (unitless)
BW	=	Receptor body weight (kg)

Indoor Dust Inhalation

IDI = [(TSOW x IACW) + (TSOS x IACS)] x AI x IB / BW

where:

IDI	=	Indoor dust inhalation exposure (µg/kg body weight/d)
TSOW	=	Fraction of time spent outdoors at assessed location - Winter (unitless)
TSOS	=	Fraction of time spent outdoors at assessed location - Summer (unitless)
IACW	=	Indoor air chemical concentration - Winter (µg/m^3)
IACS	=	Intdoor air chemical concentration - Summer (µg/m^3)
AI	=	Amount of air inhaled (m^3/d)
IB	=	Inhalation bioavailability (unitless)
BW	=	Receptor body weight (kg)

Outdoor Soil Ingestion

OSI = [FTS + (FTW x WCF)] x IEOS x SSC x ASI x OSB / BW x (AETW / HPW)

where:

OSI	=	Outdoor soil ingestion exposure (µg/kg body weight/d)
IEOS	=	Fraction of ingestion exposure *via* outdoor soil (unitless)
AETW	=	Accumulated exposure time per week (hrs/wk)
HPW	=	Number of hours per week (168 hrs/wk)
FTS	=	Fraction of time in summer season (unitless)
FTW	=	Fraction of time in winter season (unitless)
WCF	=	Winter covering factor (unitless)
SSC	=	Surficial soil chemical concentration (µg/g)
ASI	=	Total amount of soil and dust ingested (g/d)
OSB	=	Oral bioavailability from soil source (unitless)
BW	=	Receptor body weight (kg)

Indoor Dust Ingestion

IDI= [(FTS x IDCS) + (FTW x IDCW)] x IEOS x ASI x ODB / BW x (AETW / HPW)

where:

IDI	=	Indoor dust ingestion exposure (µg/kg body weight/d)
IEOS	=	Fraction of ingestion exposure *via* indoor dust (unitless)
AETW	=	Accumulated exposure time per week (hrs/wk)
HPW	=	Number of hours per week (168 hrs/wk)
FTS	=	Fraction of time in summer season (unitless)
FTW	=	Fraction of time in winter season (unitless)
IDCS	=	Indoor dust chemical concentration - Summer (µg/g)
IDCW	=	Indoor dust chemical concentration - Winter (µg/g)
ASI	=	Total amount of soil and dust ingested (g/d)
ODB	=	Oral bioavailability from dust source (unitless)
BW	=	Receptor body weight (kg)

Outdoor Dermal Exposure

ODE = [(TSOW x AESW x WCF) + (TSOS x AESS)] x SAF x SSC x DB / BW

where:

ODE	=	Outdoor dermal exposure (µg/kg body weight/d)
TSOW	=	Fraction of time spent outdoors at assessed location - Winter (unitless)
TSOS	=	Fraction of time spent outdoors at assessed location - Summer (unitless)
AESW	=	Area of exposed skin on receptor - Winter (m^2)
AESS	=	Area of exposed skin on receptor - Summer (m^2)
SAF	=	Soil adherence factor ($g/m^2/d$)
WCF	=	Winter covering factor (unitless)
SSC	=	Surficial soil chemical concentration (µg/g)
DB	=	Dermal bioavailability (unitless)
BW	=	Receptor body weight (kg)

Indoor Dermal Exposure

IDE = [(TSIW x AESW x IDCW) + (TSIS x AESS x IDSC)] x SAF x DB / BW

where:

IDE	=	Indoor dermal exposure (µg/kg body weight/d)
TSIW	=	Fraction of time spent indoors at assessed location - Winter (unitless)
TSIS	=	Fraction of time spent indoors at assessed location - Summer (unitless)
AESW	=	Area of exposed skin on receptor - Winter (m^2)
AESS	=	Area of exposed skin on receptor - Summer (m^2)
SAF	=	Soil adherence factor ($g/m^2/d$)
IDCS	=	Indoor dust chemical concentration - Summer (µg/g)
IDCW	=	Indoor dust chemical concentration - Winter (µg/g)
DB	=	Dermal bioavailability (unitless)
BW	=	Receptor body weight (kg)

Drinking Water Exposure

DWE = (AWC x CWS x OWB) x (AETW / HPW) / BW

where:

DWE	=	Drinking water exposure (µg/kg body weight/d)
AWC	=	Amount of water consumed per day (L/d)
CWS	=	Chemical concentration in assessed water supply (µg/L)
AETW	=	Accumulated exposure time per week (hrs/wk)
HPW	=	Number of hours per week (168 hrs/wk)
OWB	=	Oral bioavailability from water source (unitless)
BW	=	Receptor body weight (kg)

Home Garden Dietary Exposure

HGE = [(ARV x RVC x FPHG) + (AOV x OVC x FPHG) + (AFJ x FJC x FFJC)] x OFB / BW

where:

HGE	=	Home garden dietary exposure (µg/kg body weight/d)
ARV	=	Amount of root vegetables consumed (g/d)
AOV	=	Amount of other vegetables consumed (g/d)
AFJ	=	Amount of fruit and juices consumed (g/d)
FPHG	=	Fraction of produced from home garden (unitless)
FFJC	=	Fraction of fruit and juices consumed (unitless)
RVC	=	Chemical concentration in root vegetables (µg/g wet weight)
OVC	=	Chemical concentration in other vegetables (µg/g wet weight)
FJC	=	Chemical concentration in fruit and juices (µg/g wet weight)
OFB	=	Oral bioavailability from food sources (unitless)
BW	=	Receptor body weight (kg)

General Food Basket Exposure

FBE = DIFS x OFB

where:

FBE	=	General food basket dietary exposure (µg/kg body weight/d)
DIFS	=	Estimated daily intake from food sources (µg/kg body weight/d)
OFB	=	Oral bioavailability from food sources (unitless)

2.3 Hazard Assessment

The toxic potency of a chemical, or the ability to produce any type of damage to the structure or function of any part of the body, is dependent on the inherent toxicity of the chemical itself (*i.e.*, its ability to enact the mechanism of toxicity), as well as the ability of the chemical to reach the site of action (*i.e.*, bioavailability). The toxicity of a chemical depends on the amount of chemical taken into the body (referred to as the "dose") and the duration of exposure (*i.e.*, the length of time the person is exposed to the chemical). For every chemical, there is a specific dose and duration of exposure necessary to produce a toxic effect in humans (this is referred to as the "dose-response relationship" of a chemical). The dose-response principle is central to the risk assessment methodology, and is characterized for a certain chemical *via* observations of the toxicological effects resulting from experimental exposures of organisms, either in the environment, from various point and non-point sources, or in the laboratory, under controlled conditions (Doull *et al.*, 1980; FDA, 1982). From these data, the level at which no adverse effects would be expected to occur (*i.e.*, the toxicological criterion, expressed as μg chemical/kg body weight/day), may be estimated, with the use of extrapolation factors to allow interspecies and interindividual extrapolation of the dose-response relationship.

The development of a toxicological criterion must incorporate consideration of factors which affect the impact of a given chemical. These factors may be scenario-specific, such as variation in duration or levels of exposure, which may result in impact on different target organs; this requires that the toxicological criterion is derived from "realistic" exposures representative of those occurring under practical conditions. For many chemicals, the toxic endpoint is also dependent on the route of exposure, as exposure *via* different routes may impact tissues only at the site of entry. In such a case, different toxicological criteria would be recommended for the different routes of exposure. Toxic potency may be modified by organism-specific factors such as the ability to resist, repair or adapt to the toxic impact, depending on the age, sex, species, *etc.*, of the receptor. In these situations, separate toxicological criteria might be used to ensure protection of sensitive sub-populations. In the final analysis, toxicological criteria for chemicals are based on a consensus opinion and peer-reviewed by a number of experienced scientists with expertise in a wide range of scientific disciplines.

One of the most important factors in determining exposure of target tissues to chemicals is bioavailability, or the proportion of a chemical dose entering the blood stream following administration *via* a particular route (*i.e.*, oral, inhalation or dermal). The bioavailability of a chemical is dependent on the chemical form, environmental medium, as well as the tissue/animal species with which the chemical interacts. Adjustments for bioavailability are only made when the critical effects are systemic in nature (*i.e.*, following entry into and distribution by the bloodstream, as opposed to occurring at the site of entry [lungs, skin, gut]). Bioavailability adjustments are made if:

- the toxicological criterion is based on a route of entry different from the estimated exposure (*i.e.*, when the published toxicological criterion is based on ingestion exposure and calculated exposures are for inhalation); or

- the medium of administration results in different bioavailabilities (*e.g.*, ingestion in drinking water versus ingestion in soil); or

- if the bioavailability of the chemical, based on the particular study animal/receptor, is different from that of the assessment receptor (*i.e.*, if the published toxicological criterion were based on a study using mice, the receptor is a human, and there are reported bioavailabilities for each).

In these cases adjustment for bioavailability is an essential step in determining appropriate toxicological criteria for use in comparing to route-specific exposures, in order to ensure that comparisons (*i.e.*, in risk characterization) are made either for internal ("bioavailability-adjusted") doses and limits relevant to the species or population being assessed, or route-specific doses and limits. It allows normalization of exposures with respect to exposure route, the calculation of total exposures through all routes, and allows the bioavailable doses to humans to be compared with bioavailable doses (*i.e.*, toxicological criteria) determined from animal studies or human epidemiological data. In cases where the route of the estimated exposure and the toxicological criterion are the same, the bioavailability adjustment is, in effect, cancelled out by use on both sides of the risk characterization equation.

Derivation of Toxicological Criteria

For each of the chemicals of concern, a toxicological assessment was conducted, involving identification of mechanism of action and relevant toxic endpoints, and determination of receptor-specific toxicological criteria. In many cases, such an assessment has been made by a regulatory agency, such as Health Canada or the U.S. Environmental Protection Agency (U.S. EPA).

Two basic and quite different methods are commonly recognized by regulatory agencies for the estimation of toxicological criteria for humans, and are applied depending on the mode of toxic action of the compound (FDA, 1982; U.S. EPA, 1989). These are the threshold approach (or the no-observed-adverse-effect levels [NOAELs] - extrapolation factor approach) and the non-threshold (or the mathematical model-unit risk estimation approach).

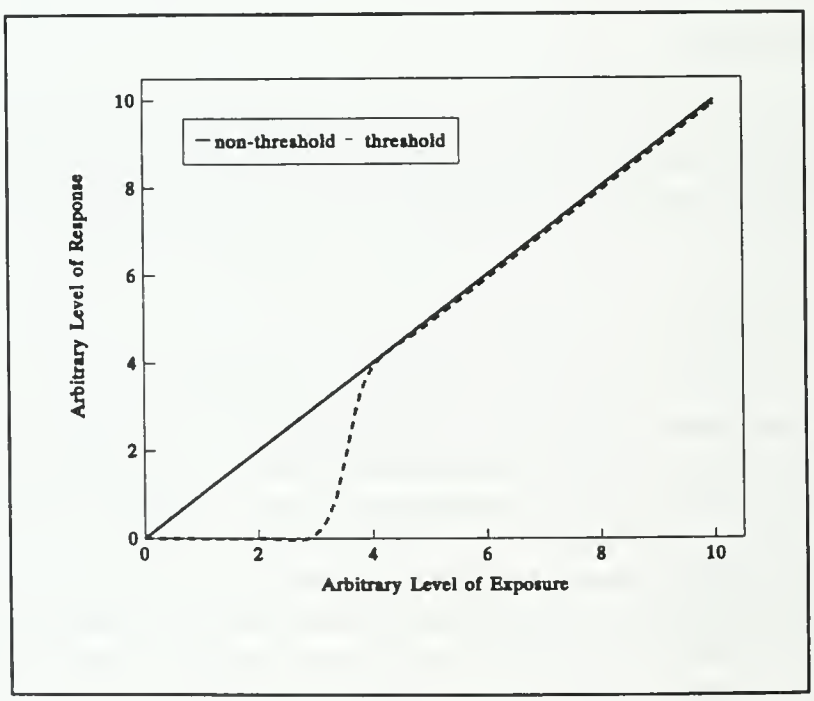
For chemicals with threshold-type dose-response relationships (*i.e.*, for which NOAELs can be determined), it is assumed, for practical purposes, that there is a threshold of exposure below which the risk of adverse effects is essentially zero, and no adverse effects will occur. This threshold is commonly referred to as a reference dose (RfD), or allowable daily intake (ADI). Conservative estimates of this threshold are based on an experimentally-determined NOAEL, with the application of low-dose extrapolation factors. These factors are also called "safety factors" or "uncertainty factors" (FDA, 1982; U.S. EPA, 1989; Health Canada, 1993).

and their magnitude is dependent on the level of confidence in the use of available data as a basis for extrapolation to the exposure scenario of the risk assessment. This confidence is dependent on differences in species and duration of exposure, safety of sensitive species and individuals, and the quality of available data (*i.e.*, the weight of evidence of the supporting data).

The mathematical model-unit risk estimation approach is based on the assumption that "absolutely no risk of the occurrence of adverse effects" would only be observed when the rate of exposure or dose was zero. This approach, generally applied to genotoxic carcinogens, yields an estimate of a cancer slope factor or unit risk cancer potency estimate (q_1^*), from which a risk-specific dose (RsD) is calculated. Since, in theory, any exposure has the potential to cause damage, the RsD specifies a dose or exposure level associated with a certain level of risk of the occurrence of an adverse health effect; this limit is thus based on the consideration of an "acceptable" level of risk for a given toxic endpoint. For example, the OMOE has indicated that carcinogenic risk levels less than one-in-one million would be considered acceptable (OMOE, 1997), that is, risks which are associated with an increased risk of cancer in one person out of one million people.

The following figure provides a graphical representation of threshold and non-threshold type dose response relationships.

Figure 2-1 Dose-Response Relationships



The following conservative assumptions are used in development of toxicological criteria for the chemicals of concern:

- For genotoxic carcinogens, it was assumed that no repair of genetic lesions occurs, and that, therefore, no threshold can exist for chemicals that produce self-replicating lesions. However, the existence of enzymes that routinely repair damage to DNA are well documented in the scientific literature, and the potential adverse effects arising from damage to DNA would only be observed if the ability of these repair enzymes to "fix" the damage was exceeded.

- Large safety factors (*i.e.*, 100-fold or greater) were used in the estimation of the RfD for threshold-type chemicals. These safety factors were applied to exposure levels from studies where no adverse effects are observed (*i.e.*, to the NOAEL). Thus, exceeding the toxicological criterion does not mean that adverse effects would occur, rather it means that the safety factor beyond the no-effect exposure is somewhat reduced.

- Humans were assumed to be the most sensitive species with respect to toxic effects of chemical. However, for obvious reasons, toxicity assays are not generally conducted on humans, so toxicological data from the most sensitive laboratory species were used in the estimation of toxicological criteria for humans.

2.4 Risk Characterization

Risk characterization for chemicals with a threshold-type dose response consists of a comparison of the toxicological criteria (*i.e.*, the rate of exposure that would not produce adverse effects) against the total estimated exposure. This comparison is expressed as an Exposure Ratio (ER) and is calculated by dividing the predicted exposure by the toxicological criterion, as indicated in the following equation:

$$Exposure\ Ratio = \frac{Bioavailability\text{-}Adjusted\ Estimated\ Exposure}{Bioavailability\text{-}Adjusted\ Exposure\ Limit}$$

Risk characterization for chemicals with a non-threshold-type dose response (*i.e.*, carcinogens) consists of a calculation of the Cancer Risk Level (CRL), which is defined as the predicted risk of an individual in a population of a given size developing cancer over a lifetime. The CRL is expressed as the prediction that 1 person per ***n*** people would develop cancer, where the magnitude of ***n*** reflects the risks to that population; for example, if the CRL is 1 person per 10, the predicted risks of any individual developing cancer would be higher than if the CRL is 1 per 1000. The following equation provides the method whereby the CRL is calculated:

Cancer Risk Level = Bioavailability-Adjusted Estimated Exposure x Bioavailability-Adjusted Cancer Slope Factor

ERs and CRLs are used to express the potential adverse health effects from exposures to the selected chemicals for several reasons:

- to allow comparisons of potential adverse effects on health between chemicals and different exposure scenarios (*e.g.*, typical Ontario *versus* site-specific conditions);
- to estimate potential adverse effects on health from exposures to mixtures of chemicals that act on similar biological systems (*e.g.*, all chemicals that cause liver toxicity, or kidney toxicity, or respiratory tract cancers); and,
- to simplify the presentation of the SSRA results so that the reader may have a clear understanding of these results, and an appreciation of their significance.

2.4.1 Amortization of Exposure: Carcinogens

In the case of carcinogens, because the endpoint is considered to be incremental lifetime cancer risk, the exposure period upon which the toxicological criterion is based is inherently a lifetime (*i.e.*, 70 years). Therefore, for exposure periods less than a lifetime, the exposure is amortized, or averaged over the entire lifetime. In this way, if an individual is exposed for 5 years, the exposure estimate used for comparison to the toxicological criterion would be multiplied by a factor of 5/70, the amortized exposure.

2.4.2 Consideration of Chemical Mixtures

Concomitant exposures to more than one chemical may result in interactions of the toxicological effects; this may result in a combined toxicity which is equal to the sum of toxicities of the individual chemicals (an additive interaction), greater than the sum (synergism or potentiation) or less than the sum (antagonism). In general, toxicological interactions of chemicals are dependent on the chemicals present, their mode of action and their concentrations. Most non-additive interactions can only be demonstrated at relatively high exposures, where clear adverse effects are observed. Such interactions have not been observed or quantified at the relatively low rates of exposure typical of those associated with most environmental situations (NAS, 1983; Krewski and Thomas, 1992).

2.4.3 Evaluation of Exposure Ratios and Cancer Risk Levels

Using the deterministic approach, as conducted in the current assessment, ERs and CRLs are given as point values. Using the probabilistic approach, the results of the human health assessment are expressed as a frequency distribution forecast or profile. The frequency distribution forecasts provide the full range of percentile confidence intervals for each chemical, hypothetical individual and scenario evaluated. For this assessment, the 5^{th} to 95^{th} percentile confidence intervals were selected for presentation of results. For the probabilistic assessment, most parameters used have incorporated a distribution of the expected range of values, rather than a single point estimate. Consequently, the final results of the distribution

forecast enable a greater use of available information than assessments that consider only single, point estimate values. By incorporating a range of values for parameters, rather than a single value, the influence of variability on different exposure and hazard parameters can be estimated and its significance evaluated. Generally, the focus of the human health assessment is based on the upper 95th percentile of the distribution forecast, although it is also important not to lose sight of the entire distribution forecast by providing the 5^{th} to 95^{th} percentile confidence intervals and to compare the distribution forecast between different scenarios (*e.g.*, site versus typical Ontario).

The evaluation of ERs and CRLs can be applied with greatest confidence to situations where comparisons are made between the ERs/CRLs of two or more independent exposure scenarios. From such comparisons, the incremental difference in the potential for occurrence of adverse health effects between the two or more different scenarios (*e.g.*, site versus typical Ontario) can be assessed with reasonable confidence since the same methodologies are used in addressing each situation. Most of the uncertainties in such comparative health assessments are related to the accuracies in estimating the concentrations in various environmental media that affect the different exposure pathways, and in the estimation of the toxicological criterion based on the toxic potency of the chemical. Since the assumptions used in the estimation of a toxicological criterion, in various exposure modifying factors and in different hypothetical individual characteristics, are common across scenarios that are being compared, any uncertainties in these parameters tend to cancel between the different scenarios.

For ERs, technically, if the total exposure to a chemical is equal to or less than the toxicological criterion, then the ER would be 1.0 or less, and no adverse health effects would be expected. For human exposure to non-carcinogens, the toxicological criteria represent the level of total exposure, derived from multisource and multimedia exposures, which would not result in adverse health effect, regardless of the source or route of exposure. There are two options to address this concern. If the risk assessment addresses risks associated with a single source and a limited number of environmental pathways, the selection of an ER of 1.0 as a benchmark to indicate that exposure does not exceed the toxicological criterion is not valid. In an attempt to address this problem, the OMOE has apportioned 20% of the total exposure to any one source or pathway (OMOE, 1997). This means that the total toxicological criterion must also be apportioned for the single source (*i.e.*, the contaminated site) under consideration. ER values for non-carcinogens which are less than 0.20 are considered to represent a situation in which site-related exposures account for less than 20% of the toxicological criterion, and no adverse effects are expected to be associated with the estimated level of exposure. However, if the risk assessment included estimation of exposures not associated with the site being assessed, as discussed in Section 2.2.1, then risk evaluation is based on the consideration that all significant sources of exposure are included in the assessment, and that the total exposure of each receptor is being evaluated. Therefore, the entire toxicological criterion can be compared to exposure in risk characterization, and is thus considered the "acceptable level" of exposure.

CRLs, as discussed above, represent the predicted incremental risk of cancer over a lifetime to an individual member of a population of a given size, and is expressed as a risk level (*e.g.*, 1 person per ***n***). In order to evaluate this, then, the CRL may be compared to a benchmark risk level that is considered to be acceptable. Negligible or *de minimis* cancer risk levels are generally considered to be $1x10^{-4}$ to $1x10^{-6}$; however, evaluation of predicted cancer risks for a population must also consider predicted risks for a background or "typical" population, since "typical" populations are considered to be without undue cancer risks, predicted CRLs for these receptors can provide a valid "acceptable level" of risk, given the commonality of methods in exposure and risk assessment.

In cases where the estimated exposures or risks are less than the acceptable level, it can be concluded that no observable adverse health effects would be expected to occur, considering the more sensitive members of the population or the majority of the exposure scenarios considered in the assessment. Exposures that are substantially less than the acceptable level are not considered to require re-evaluation.

If exposures or risks are predicted to be within the same magnitude as the acceptable level (*e.g.*, ER values in the range of 10-fold less than to somewhat greater than 1.0), this would indicate situations that require re-evaluation of model parameters (*e.g.*, chemical concentration estimates, exposure parameters, and toxicological criteria) before the potential risks to health can be characterized. Consideration must be given to the possibility of adverse health effects, but such exceedences are not necessarily indicative of potential risks, as they may reflect overestimation of risk due to the use of overly conservative estimates (*e.g.*, overestimating exposures through use of maximum soil ingestion rates). This procedure is followed to ensure the predicted potential impacts on human health were not over- or under-estimated. The data may be interpreted as indicating that given the conservatism of the assessment, no adverse health effects would be expected, or this evaluation may indicate that further action (*i.e.*, progression to a probabilistic risk analysis, or recommendation of remediation) is required.

When predicted exposures or risks are greater than the acceptable level, this may indicate the potential for adverse effects in sensitive individuals or in some of the exposure scenarios considered. Re-evaluation of such ERs/CRLs is extremely important since both the exposure estimation procedures and the toxicological criteria are based on a series of conservative assumptions, particularly when considering the maximum point estimate from deterministic analyses or upper 95^{th} percentiles of a probabilistic forecast. A sensitivity analysis facilitates the re-evaluation by focusing on the proportional contribution of various parameters to the final ER/CRL value. Once the major contributing model parameters have been identified, they can be evaluated to assess whether health risks have been either under-estimated or grossly over-estimated. A certain amount of over-estimation of risk is inherently built into the risk assessment process. For example, in cases where there is considerable uncertainty in the data such as the determination of toxicological criteria for cancer causing chemicals (*e.g.*, arsenic), a conservative dose-response extrapolation model is used to derive the toxicological criterion to ensure the protection of human health. In probabilistic analyses, the estimates of potential adverse effects on human health at the upper end of the distribution forecast (*e.g.*,

the 95th percentile) represent the combination of numerical parameter values that occur infrequently based on the frequency distribution functions used for the various parameter values. The re-evaluation of the basis for these values at the upper end of the frequency distribution function must be conducted prior to recommending actions based on these estimates. The outcome of this analyses may include recommendations regarding progressing to a probabilistic analyses, or for the need for remedial activities.

2.5 Risk Management Recommendations

If the results of the risk characterization indicates that there are unacceptable risks posed to the receptors of concern, then recommendations on mitigation of those risks are made. Recommendations may provide a mechanism for altering or removing exposure pathways which make significant contributions to the risk estimate. For example, if contact with surface soils are driving the risks, depending on the current and future uses of the land, it may be appropriate to simply put a layer of asphalt over the soil, thereby preventing such soil contact and mitigating the risk. In other cases, such as for parkland, it may be necessary to remediate the site through removal of contaminated media. Generally, in such a case, risk management criteria, or the concentration of a chemical of concern which would not pose unacceptable risk to critical receptors, calculated from the results of the risk characterization, would be used to guide remediation activities.

3.0 UNCERTAINTY AND SENSITIVITY ANALYSIS

3.1 Introduction

Environmental risk assessments typically undertake the simulation of highly complex environmental, biological, and physiological processes through which chemicals within the environment impact upon given biological receptors (*i.e.,* humans or wildlife). Given the complexity of these processes, quantification of the potential risk associated with these impacts include varying degrees of inherent uncertainty, typically dependent on the underlying parameters and methodologies used within the risk assessment.

When discussing the uncertainty in the risk assessment process, it is important to distinguish between variability and uncertainty in the data and overall methodology. Variability represents the heterogeneity or diversity in a well-characterized population, which is usually not reducible through further measurement or study (*e.g.,* body weight varies on an individual basis). Uncertainty represents a fundamental lack of knowledge about a poorly characterized phenomenon, which is sometimes reducible through further measurement or study (*e.g.*, potential error in the weighing methodology used to determine body weight). However, due to the typical difficulty in distinguishing between variability and uncertainty, and individual quantification of each, the two are sometimes combined under the overall banner of uncertainty.

Many definitions of uncertainty emphasize subjectivity, or involve a judgmental process. For example, some sources of uncertainty are amenable to quantification *via* data analysis (*e.g.*, random sampling error, measurement error), while other sources of uncertainty involve more explicit judgements (*e.g.*, representativeness of overall data, or lack of data).

Describing inherent uncertainty associated with the estimated exposure and its collated risk level is an important part of the risk assessment process, and is normally estimated through the use of a uncertainty analysis. In addition to the risk estimates, it is important for risk assessors and managers to understand the uncertainties inherent within the assessment methodology, assumptions, and data. Uncertainty analyses consist of a qualitative or quantitative summary of the uncertainties associated with the risk assessment and a prediction of how these uncertainties are expected to affect the final outcome. The level of uncertainty present within a given assessment is also dependent upon the methodologies used to calculate overall risk.

3.2 Deterministic *versus* Probabilistic Assessment Methodologies

Risk assessments may employ a *deterministic* approach, where a single point estimate value (*e.g.,* mean, median, 95th percentile) is used for parameter input, or a *probabilistic* (stochastic) approach, where probability distribution functions (a statistical distribution of values used to represent uncertainty or variability in a parameter) are used for the input variables. After defining the goals and scoping the complexity of the risk assessment problem, the risk assessor should determine whether deterministic, probabilistic or a

combination of such analytical approaches should be employed. It is important to establish this as soon as possible since the outcome of the decision may require new data or different techniques to be employed in subsequent phases of the risk assessment.

3.2.1 Deterministic Assessment

The traditional approach to mathematical modelling in a human health risk assessment has been deterministic. The outcome of a deterministic risk assessment model is a point estimate of risk with no definition of its underlying distribution. Such a risk assessment does not provide a quantitative understanding of the likelihood that the risk estimate accurately represents the mean, mode, median, or any specific percentile range of the underlying distribution. Consequently, there is no quantitative estimate of whether the point estimate of risk is an overstatement or understatement of the average or reasonable maximum potential risk. It is important to note that, given the conservative nature of the assessed parameters (*e.g.*, assumed worst-case scenario values) it is highly unlikely that an assessment would underestimate the potential risk. However, the lack of quantified uncertainty associated with a deterministic risk estimate may compromise the quality of risk management decisions when the estimated risk suggests that a marginal level of concern exists.

Point estimations of health risks have three major limitations:

- The selection of a mixture of moderate, conservative and worst-case assumptions leaves assessors, managers and the general public with no clear understanding of the degree of conservatism in the estimates of potential human health impacts (Thompson *et al.*, 1992); thus making it difficult to put these estimates into perspective relative to real-world conditions;

- If the input variables are individually set great enough to avoid underestimations of potential adverse effects, the overall scenario considered will rarely (if ever) happen under real world conditions (Thompson *et al.*, 1992; Whitmyre *et al.*, 1992a). This feature may make the risk assessment highly unrealistic and lead to gross misconceptions by the public and decision-makers regarding the validity and overall meaning of the results of the assessment; and

- It is not possible to evaluate the validity of, or uncertainty in, the point estimates of potential human and/or ecological health impacts using traditional sensitivity analysis procedures because many of the variables are at, or near their maxima (Thompson *et al.*, 1992).

3.2.2 Probabilistic Assessment

Probabilistic (stochastic) approaches quantify overall uncertainty (including both variability and uncertainty) by employing probability distributions for the various input parameters which then results in a distribution of risks and corresponding probabilities. This additional

information may be desirable in various risk management decisions, particularly when the risk estimates are of a magnitude that is close to a concern level.

Uncertainties in estimates of potential human health impacts of chemical exposure arise from both the exposure estimates (Thompson *et al.*, 1992; Whitmyre *et al.*, 1992a,b) and hazard assessment of chemicals (Thompson *et al.*, 1992). Decision analysis and information analysis techniques that use probabilistic methods (*e.g.*, probability-based methods such as Monte Carlo simulation) are applied to address some of the weaknesses of point estimation methods. Probabilistic methods enable the estimation of both point values and full distributions of exposures and potential impacts on human health (Whitmyre *et al.*, 1992a,b). The numerical model used then calculates a value of each possible outcome, and also indicates the probability of each outcome. Therefore, exposure estimates can be expressed as discontinuous probability distributions made up of specific numbers of different discrete numerical values. When coupled with uncertainty analysis, these approaches allow the incorporation of the full range of statistical data for each parameter in the exposure and hazard assessment algorithms (Thompson *et al.*, 1992; Whitmyre *et al.*, 1992a,b).

These probabilistic analytical approaches, when appropriately used, enable greater use of available information than point estimate procedures, incorporate weight-of-available-evidence considerations of the information used and the results obtained, and can include modifying factors based on professional judgement that are considered standard practise in risk assessment. The main purpose of using such approaches is to provide useful measures of variability and summary statistics of the estimates of potential adverse impacts on human health. The value of such techniques is that they enable the use of representative exposure factor ranges, distributions and statistics in combination with probabilistic analyses in the human health assessment.

In using probabilistic analytical techniques in risk assessment, considerable care must be exercised in the adoption of probability distributions for the model variables. Models for the treatment of uncertainty can be based on probabilistic, parametric or switch-over assessment techniques. Parametric sensitivity analysis refers to the examination of the effect on a model output by deterministic changes to the uncertainty quantity. Switch-over analysis techniques involve the analytical or numerical examination of the model to determine the specific magnitude of the input variable that produces optimal decision changes in model output. Probabilistic analysis involves the determination of the amount of uncertainty in model conclusions attributable to a particular input parameter, using correlation, rank correlation, regression and other statistical means (Morgan *et al.*, 1990).

Generally, probabilistic methods indicate that risks estimated using deterministic approaches of the same scenarios lie above the 99th percentile in terms of a probabilistic estimate (Whitmyre *et al.*, 1992b). Without information on the variability and uncertainty in the risk assessment results, the degree of conservatism believed to be inherent in point estimates can only be intuitively assumed. However, it is important to remember that every assumption is selected to be conservative in nature. Thus, while the degree of conservatism inherent in the

assessment results is assumed, there is a high degree of certainty that the assessment over-estimates, rather than under-estimates, health risks.

3.3 Evaluating Assessment Uncertainty

Given the inherent problems in interpreting deterministic risk assessments, it is important to have an understanding of when it is most appropriate to perform a risk assessment either deterministically, probabilistically, or using both methods of analysis.

Deterministic modelling can be especially effective as a first-cut screening tool or for use in small scale risk assessments with limited budget or constraints in reporting schedule, because it is generally conservative (*i.e.,* risk estimates will be biased on the side of safety) and requires less resources and time to perform than probabilistic methods. When detailed communication of the uncertainties in risk estimates is not required (*e.g.,* when there is a low degree of public interest), or low uncertainty exists, deterministic methods are again suitable because they can provide the needed information in a less costly and shorter time frame.

However, certain conditions exist where the use of probabilistic modelling provides distinct advantages because of its ability to provide greater insight on risk estimates through quantification of variabilities and uncertainties. Thus, where there is a high degree of parameter-specific uncertainty or where there is a high degree of public interest such as controversy over the relevance or meaning of a risk estimate to public health (*i.e.,* where qualitative estimates of uncertainty are not acceptable for comprehension or communication purposes), probabilistic methods are more desirable. They provide added insight by describing the risk in terms of the *average-exposed person* or the person in the 95th percentile of exposure (upper bound estimate), for example, or can differentiate between the proportion of total risk presented by individual pathways. Probabilistic approaches are also desirable where the deterministic result is close to the action level because in these cases risk managers could significantly overestimate actual risk and therefore run the chance of making erroneous decisions which do not minimize risk. Where initial risk calculations are conducted using questionable assumptions, uncertainty analysis can assist in refinement of the model assumptions and thereby leading to more realistic risk estimates. Projects involving a small number of chemicals, scenarios and/or exposure pathways are more amenable to probabilistic methods than complex assessments because they minimize the resources required in developing models and probability distributions. However; if resources are not a constraining factor, probabilistic methods can be applied equally well to complex situations. In such cases probabilistic approaches can facilitate a value-of-information analysis whereby uncertainty and sensitivity analyses are used to focus on key parameters when planning data collection or evaluating remediation alternatives and therefore save significant time, money, and resources.

Probabilistic modelling allows one to conduct effective sensitivity/uncertainty analyses that show which model parameters are contributing most to the overall uncertainty in the result. One can then focus on such parameters and evaluate whether the uncertainty is reducible (*i.e.*, is due to lack of knowledge) or unreducible (*i.e.*, is due to inherent variability). Further

sampling, for example, could reduce statistical uncertainty about the distribution of a given parameter. But, because the environment is inevitably patchy in a spatial and temporal sense, the variability inherent in the distribution of contaminant concentrations cannot be reduced (*i.e.*, contaminant concentration is not a point value, but is a distribution of values). Value-of-information analysis consists of taking such considerations into account, along with the cost of any proposed effort to reduce uncertainty. If the benefit of the effort is expected to exceed the cost, the effort is deemed to have value. One of the principles of value-of-information analysis is that more information, contrary to conventional wisdom, is not always better. If additional information is obtained in the absence of an expected project benefit, that information results in a waste of project (and potentially program) resources.

Typically, the choice of methodologies follows a step-wise process, by which the data is screened using conservative deterministic methodologies. Should these results demonstrate no significant risk to the assessed receptors, than the process may stop here. However, should a potential risk be predicted, a more realistic and evaluative assessment may be conducted using probabilistic assessment methodologies.

3.4 Sources of Assessment Uncertainty

It is important to classify the uncertainty of values within the assessment in terms of the category the values represent, since this will determine how the uncertainty should be evaluated. Although subjective probability distributions are often used to describe uncertainty, the probabilistic treatment of uncertainty is appropriate for only types of information that have "empirical or chance" properties (*i.e.*, they are estimates of some "true" value). Decision, value or policy variables, on the other hand, are quantities over which the decision maker has control. Probability distributions should not be assigned to decision variables, since the "true" value of the variable is not a constant, but is defined by the decision maker. The uncertainty of decision variables is better analysed by other methods (*e.g.*, switch-over analyses). Model domain parameters are decision variables, and should not be "assigned" probability distribution functions (Morgan *et al.*, 1990). Fiering *et al.* (1984) also discuss the problems of increases in the degree of uncertainty arising from smaller uncertainties linked in chains of random variables.

Typically, there are four main sources of uncertainty within a risk assessment: i) parameter uncertainty; ii) empirical property uncertainty; iii) model uncertainty; and, iv) decision rule uncertainty. A fifth source of uncertainty can also be found as part of the toxicological evaluation within the hazard assessment.

3.4.1 Parameter Uncertainty

Parameter uncertainty includes random measurement and systematic error, statistical variation, subjective judgement, and inherent randomness or unpredictability (Vesely and Rasmuson, 1984; Covello *et al.*, 1987; Morgan *et al.*, 1990; U.S. EPA, 1992). Typically, the uncertainty surrounding the parameters used to describe chemicals and receptors in the

assessment has the greatest potential impact upon the validity of the assessment, yet is generally the easiest to quantify.

Parameters such as soil ingestion, body weight, and soil adherence factors play an important role in the calculation of potential exposures arising from contaminant concentrations in the soils surrounding the site. Parameters such as dermal and oral bioavailability, and the fraction of time spent on-site, have a small but still significant impact on the overall model outcome. Thus, in order to ensure risks associated with these land uses are not underestimated, it is important to select receptors that would be at greatest potential risk from a site. These would include those receptors with the greatest probability of exposure to chemicals from a site and those that have the greatest sensitivity to the chemicals of concern.

The correlation of various biological parameters is one method of minimizing inherent parameter uncertainty within the assessment. The adoption of correlations for bivariant parameters is required in the Monte Carlo analysis to avoid the selection of "paired" parameters from frequency distributions that are not biologically, chemically or physically feasible (Whitmyre *et al.*, 1992b). For example, a correlation of 0.67 is applied to body weight and breathing rate to ensure that the selection of body weight values at the extremes of the distributions assigned are not paired with respiratory volumes at the opposite extremes of their distributions. In other words, a 100 kg receptor could not function physiologically at a breathing rate from the lower end of its distribution function (*e.g.*, about 4.7 m^3/d). Other model parameters that are typically correlated are body weight and drinking water consumption, body weight and exposed surface area, and body weight and food consumption.

3.4.2 Empirical Property Uncertainty

Variability in empirical properties are due to uncertainty in measurement (*e.g.*, sampling from a frequency distribution), and/or related to incomplete scientific or technical information (Covello *et al.*, 1987; Morgan *et al.*, 1990; Fiering *et al.*, 1984). Uncertainty due to variability related to sampling can be reduced by disaggregation (Morgan *et al.*, 1990) (*i.e.*, dividing age groupings into smaller intervals to reduce variability in body weight). Scientific uncertainty can only be reduced by gathering additional data, or improving the methodology by which one collects the data. In cases where data was lacking or insufficient (*e.g.*, physical characteristics of the soil at the site), worst-case values are usually assumed.

3.4.3 Model Uncertainty

Model uncertainty related to the limitations of numerical models in representing the real world, and arising from surrogate variables, excluded variables, abnormal conditions and incorrect model assumptions and form (Vesely and Rasmuson, 1984; Morgan *et al.*, 1990; U.S. EPA, 1992). The estimates of variables used as model parameters are ones that were considered realistic and conservative in nature. As such, there is confidence that the Exposure Ratio results are accordingly realistic and conservative.

For example, based upon past experience, the model typically used to predict soil gas concentrations beneath the structure (*i.e.*, the model recommended by Johnson and Ettinger, 1991) has a degree of inherent model uncertainty, and may overestimate actual concentrations by a considerable degree. Given the above, results of a risk assessment using this model may overestimate actual risks by a considerable degree, but will not underestimate potential health risks.

3.4.4 Decision Rule Uncertainty

Decision rule uncertainty is related to the measure used to describe risk. It is related to ambiguity or controversy in risk acceptability, perceptions, and social objectives or attitudes (Covello *et al.*, 1987; Morgan *et al.*, 1990). Uncertainties in scenario definition (U.S. EPA, 1992) and value parameters chosen (Morgan *et al.*, 1990) are also decision rules.

For example, decisions made as part of the site characterization phase of the assessment, and selection of potential exposure scenarios pose potential decision rule uncertainties. Unfortunately, as these types of uncertainties are inherent within the decision-making process and are typically transparent, they are difficult to quantify in a meaningful manner.

3.4.5 Toxicological Uncertainty

There is also a considerable amount of uncertainty present as part of the calculation of toxicological criteria. Many of these limits are calculated based upon animal studies, incorporating assumed animal-to-human conversion factors, or extrapolate from the lowest-observable-adverse-effect-level (LOAEL) to an NOAEL using safety factors or low-dose extrapolation methodologies. All these assumptions add to the overall uncertainty surrounding the value used as the toxicological benchmark within the risk assessment.

Unfortunately, due to the difficulty in adequately quantifying toxicological uncertainty, this potential source of error is typically not evaluated within the risk assessment process. However, as conservative safety and uncertainty factors are typically employed when establishing toxicological criteria, the resulting assessment is unlikely to underestimate potential health risk.

3.5 Quantification of Sources of Uncertainty

An essential part of the interpretation of the results of a risk assessment is the consideration and, if possible, the quantitation of sources of uncertainty. Typically, sources of uncertainty are present in each phase of the risk assessment. For example, factors which provide the basis for the exposure assessment and therefore subject to scrutiny with regard to parameter uncertainty include:

(i) media-specific concentrations, dependent on the reliability and validity of the sampling and analysis of samples and selection of representative concentrations;

(ii) modelling of environmental fate and transfer, dependent on factors such as physico-chemical properties of chemicals of concern, characteristics of media (such as fraction organic carbon, *etc.*);

(iii) modelling of receptor exposures, including characteristics of the site and/or receptors (such as rates of groundwater migration, or food consumption rates) which impact exposure.

Similarly, the toxicological assessment may have uncertainties introduced *via* limitations of the toxicological database. The available data may require extrapolation from high dose to low dose, from subchronic to chronic duration and between individuals of the same and/or different species. The impacts of species and individual differences may be profound, and incorporate such factors as variation in pharmacokinetics and toxicological susceptibility, depending on biochemical or physiological differences due to species, age, nutritional status, *etc.* Data gaps, such as a lack of teratogenicity or carcinogenicity data, may also present a source of uncertainty in toxicological assessment.

As noted previously, the presence of uncertainty in risk assessment is addressed through the consistent use of realistic yet conservative assumptions where data are lacking. Exposure estimates are maximized *via* assumption of maximum (in deterministic analyses) or 95th percentiles (in probabilistic analyses) concentrations, consumption rates, bioavailabilities, *etc.* In toxicity assessment, conservatism is maintained through selection of data for the most sensitive species and through application of uncertainty factors in derivation of toxicological criteria (*i.e.,* for inter- or intraspecies extrapolation, for use of subchronic data, *etc.*). The consistent use of conservatism in the estimation of exposure and toxicity yields a risk assessment which may be overly conservative, but which would not underestimate risks.

In mathematical models, input values for variables can dramatically affect model output. Therefore, as a part of the model evaluation process, sensitivity analysis, or the determination of the relative influence of model variables on model output, is essential. The degree of influence of the variables in the model, as determined mathematically, can be compared with known physico-chemical, biochemical and physiological properties. Justification of the model is warranted if the degree of influence of the variables is consistent with the known behaviour of the phenomena. Typically, sensitivity analysis will include an examination of the importance of exposure pathways to the determination of risk, and the role of various parameters in determining the magnitude of each pathway. Exposure and risk estimation consists of several factors: concentrations of contaminants in specific media, environmental fate and transfer, bioavailability to receptors, and toxic potency within specific receptors. Depending on the scope of the sensitivity analysis, the effort in this task may range from a simple determination of the importance of each exposure pathway to determination of the importance of characteristics of the site, chemicals and receptors which contribute to each of these factors contributing to exposure and risk.

The culmination of the uncertainty and sensitivity analysis is the identification of both the factors driving the risk assessment (*i.e.,* to which the risk estimate is most sensitive), and the

level of uncertainty inherent in the values used in that risk estimate. If the sensitivity analysis indicates that a certain parameter has a significant impact on the calculation of risk, and the uncertainty analysis indicates that the value of this parameter is unsure, then the assumptions used to derive that value may need to be re-visited. In such cases, uncertainty in the parameter may be mitigated by obtaining more data, or the uncertainty in the risk characterization may be addressed through consistent conservatism.

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CANTOX ENVIRONMENTAL

DELORO VILLAGE
EXPOSURE ASSESSMENT AND HEALTH RISK CHARACTERIZATION FOR ARSENIC AND OTHER METALS

PART 3 - REVIEW OF EXPOSURE TO ARSENIC IN THE VICINITY OF MINING OPERATIONS/SMELTERS

December, 1999

PART 3
REVIEW OF EXPOSURE TO ARSENIC IN THE VICINITY OF MINING OPERATIONS/SMELTERS

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PART 3
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1.0 SOURCES AND FATE OF ARSENIC IN THE ENVIRONMENT

1.1 Sources of Arsenic

Arsenic is naturally present in terrestrial and aquatic environments through the weathering and erosion of rocks and soils. Many regions of Canada contain naturally elevated background concentrations of arsenic in bedrock. Arsenic-enriched bedrock is relatively common in areas of precious metal deposits. For example, high arsenic content has been reported in the soils, sediments and water of precious metal deposits in Northern Ontario, Quebec, New Brunswick and Nova Scotia (*e.g.*, Boyle *et al.*,1969; Brooks *et al.*, 1982; Bottomley, 1984). The major anthropogenic sources of arsenic are base metal and gold production facilities. Other anthropogenic sources include pesticide use, wood preservation, coal-fired electricity generation, petroleum refining, antifouling paints and disposal (*e.g.*, incineration) of domestic and industrial wastes (Frank *et al.*, 1976; PACE, 1983; Henning and Konasewich, 1984; Evans *et al.*, 1985; Van Voris *et al.*, 1985; Environment Canada, 1985,1987; OMOE, 1988; Adams *et al.*, 1994). Arsenic is also released into the environment by volcanic eruptions, forest fires, the volatilization of methylarsenines from soil, and decaying plant and animal material (NRCC, 1978; Walsh *et al.*, 1979; Chilvers and Peterson, 1987).

1.2 Environmental Fate and Speciation in Environmental Media

Due to its reactivity and mobility, arsenic cycles extensively through both biotic and abiotic components of terrestrial and aquatic systems, where it can undergo a variety of chemical and biochemical transformations, including oxidation, reduction, methylation and demethylation (Cullen and Reimer, 1989). The oxidation state of arsenic is the single most important factor controlling the solubility, mobility, environmental fate, bioavailability, and toxicity of its compounds (Masscheleyn *et al.*, 1991).

1.2.1 Atmosphere

The arsenic species present in the air are dependent on the sources and on reactions with other atmospheric substances. Most of the arsenic released to the air is in the form of arsenic trioxide (As_2O_3), which is the predominant species released from smelters, fossil fuel combustion, and mineral ore roasters. The trioxide rapidly sublimates in the atmosphere to form the gaseous species, As_4O_6 (Rabano *et al.*, 1989). This gaseous compound may be adsorbed or complexed to suspended particulate matter or condense to a solid upon cooling (Cullen and Reimer, 1989; Gagan, 1979). Volatile arsines and methylarsines are also released to the atmosphere by soil and aquatic microbial processes, where they are eventually oxidized (especially in the presence of sunlight) and bound to particulates, typically as methylated As(V) species (Parris and Brinckman, 1976; NRCC, 1978). The majority of

atmospheric arsenic is associated with fine particulates (*i.e.*, less than 2.5 µm in diameter), with smaller percentages existing either in the vapour phase, or associated with coarse particulates (>2.5 µm in diameter) (Walsh *et al.*, 1979; Rabano *et al.*, 1989). The As_4O_6 species is believed to be the precursor for inorganic particulate-bound As(III) and As(V) species (Rabano *et al.*, 1989). The chemical mechanism is believed to be similar to the atmospheric reactions that occur with NOx and SOx compounds, in which weak acids NO, NO_2 and SO_2 react with alkaline coarse particles to form coarse particulate nitrate and sulfate (Rabano *et al.*, 1989). Inorganic As (III) and As (V) species (arsenites and arsenates) typically occur in the low ng/m^3 range in atmospheric particulate matter (Rabano *et al.*, 1989). Other chemical forms of arsenic found in the atmosphere in small quantities include metallic arsenic, and volatile organic arsenicals and their degradation products which result from pesticide applications. Arsenic is removed from the atmosphere *via* wet and dry deposition processes with an average atmospheric residence time of approximately 9 days (Walsh *et al.*, 1979).

1.2.2 Surface Waters and Sediments

Arsenic speciation in surface waters is highly dependent upon pH and redox potential. When As_2O_3 (or As_4O_6) is deposited into aerobic surface waters, it rapidly hydrolyzes to form mobile As(III) species, principally AsO_3^{-3} (arsenite). Arsenite is relatively unstable in aerobic waters and is slowly oxidized to form less mobile As(V) species, principally the arsenates, $HAsO_4^{-2}$ and $H_2AsO_4^{-1}$ (CEPA, 1993). Under anaerobic conditions, arsenates are reduced to arsenite (Korte and Fernando, 1991; Masscheleyn *et al.*, 1991). In deep anoxic waters, insoluble arsenic sulfides are common, while in more shallow and oxygenated waters, As(V) species tend to predominate; As (III) species tend to predominate at mid-depths under reducing conditions (Seyler and Martin, 1989). Phytoplankton blooms in surface waters can result in the biochemical reduction of arsenates to arsenite, as well as the production of methylated arsenic species (Andreae, 1978). Since arsenic does not occur as a cation in fresh surface waters, it does not complex with humic or fulvic acids, nor does it form complexes with other common anions in water to an appreciable extent (Korte and Fernando, 1991).

In general, dissolved arsenic is rapidly removed from the water column by biotic uptake, fixation by organic matter, adsorption onto iron or manganese hydroxides or clay particles, precipitation and co-precipitation (Nriagu, 1983). These removal mechanisms result in the majority of arsenic in surface waters being deposited in sediments. Sediments are a major long-term sink for arsenic, with some studies suggesting sediment retention times of up to 100 years (Nriagu, 1983; Sutherland, 1989). However, some sediment-bound arsenic may be released into pore waters and the water column by organic decomposition processes, or dissolution of iron/manganese hydroxides under anaerobic conditions resulting from sediment reburial (Nriagu *et al.*, 1987; Belzile, 1988). In addition, arsenates can be reduced to arsenites in sediments, which are subsequently methylated by microorganisms to form methylarsinic acids. These can be further reduced to yield volatile methylarsines, which are eventually released to the atmosphere (Wade *et al.*, 1993). While the production of methylarsines in sediments occurs mainly under anaerobic conditions, there is some evidence that this process can also occur under aerobic conditions (Brinckman *et al.*, 1977). The processes that lead to the methylation of arsenic by aquatic microbial species are poorly

understood (Anderson and Bruland, 1991); however, detoxification and/or energy generation have been suggested by several authors to be the driving force behind the biomethylation of arsenic (Mitchell and Barr, 1995).

1.2.3 Soils and Groundwater

Arsenic speciation in soil is influenced by complex interactions between pH, redox potential, organic content, iron oxyhydroxide (and other hydrous metal oxide) concentrations and soil particle size. The principal species present in soil are arsenites (As(III) or AsO^{3-}), arsenates (As(V) or $As_2O_4^{3-}$), and methylated arsenicals from herbicide use (*e.g.*, monomethylarsonic acid, dimethylarsinic acid). The methylated arsenicals have soil half-lives ranging from 0.5 to 2.9 years but are eventually degraded to carbon dioxide and arsenate by soil microorganisms (Hiltbold, 1975). Some soil arsenic is lost to the atmosphere *via* the microbially-mediated volatilization of arsine and methylarsines (NRCC, 1978). However, soil microbial activity also results in arsenic inputs to the soil through the mobilization of arsenic present in rocks and minerals by microbial oxidation of sulfides and ferrous iron in these minerals to sulfate and ferric iron (Tamaki and Frankenberger, 1992).

The predominant chemical species in groundwater appear to be inorganic As(V) and to a lesser extent, As(III) (Korte, 1991; Masscheleyn *et al.*, 1991). Groundwater normally contains higher arsenic concentrations than surface waters (Boyle and Jonasson, 1973). However, high groundwater arsenic concentrations can also be due to elevated arsenic content in bedrock, such as in a number of regions of Ontario, Quebec, New Brunswick, and Nova Scotia (*e.g.*, Boyle *et al.*,1969; Brooks *et al.*, 1982; Bottomley, 1984; Meranger *et al.*, 1984).

The movement of arsenic species from soil to groundwater is dependent on the properties of the arsenic species, and soil properties such as pH, redox potential, organic content, cation exchange capacity, iron oxyhydroxide (and other hydrous metal oxide) concentrations, soil particle size, and concentrations of other chemicals in the soil. Most arsenic in soils is tightly bound to iron/manganese oxides and clay particles, which reduces the amount of arsenic that can leach into groundwater or be taken up by plants (CEPA, 1993). The use of phosphate fertilizers can result in the mobilization of otherwise tightly bound arsenic in soil (Peryea, 1991). Medium to fine-grained, well drained soils can retain arsenic for decades (Veneman *et al.*, 1983). Poorly drained soils do not retain arsenic as efficiently though as flooding creates an anaerobic environment that results in the mobilization of arsenic (Masscheleyn *et al.*, 1991). Panstar-Kallio and Manninen (1997) found that more inorganic As(III) and As(V) species were mobilized from sandy soils than from humic or clay soils. In general, inorganic arsenic species have been found to be highly mobile and leachable in sandy versus higher clay content soils (Walsh *et al.*, 1977). Panstar-Kallio and Manninen (1997) also found that high pH values resulted in greater mobilization of inorganic arsenic than low pH values. However, over a pH range of 3 to 9, less than 2% of inorganic arsenic was mobilized, indicating that environmental pH changes would have to be drastic to result in the release of significant amounts of arsenic from the soil matrix. In all soil mobilization experiments conducted by the authors, As(V) species were the predominant species extracted from the soil types studied. In an earlier study, Masscheleyn *et al.*, (1991) found that alterations in the

oxidation state of arsenic, brought about by changing redox potential and pH, greatly affected its solubility in soil. At high redox levels, arsenic solubility was low and 65 to 98% of the dissolved arsenic was present as As(V). High pH values or reducing conditions resulted in the release of substantial amounts of arsenic into solution; present mainly as As(III). Under moderately reduced conditions, arsenic solubility was mainly controlled by the dissolution of iron oxyhydroxides. Therefore, when arsenic-containing wastes are released to soil, consideration should be given to maintaining a high soil redox potential and nonalkaline conditions to minimize arsenic solubility and mobility (Masscheleyn *et al.*, 1991).

1.2.4 Biota

The extensive biogeochemical cycling of arsenic results in its occurrence in virtually all living organisms. Although bioconcentration factors (BCFs) for aquatic organisms, including algae, crustaceans, and fish have been reported to be as high as several thousand, arsenic does not bioaccumulate to any great extent, nor does it biomagnify in either aquatic or terrestrial food webs (NRCC, 1978; Eisler, 1988; Adams *et al.*, 1994). In freshwater aquatic plants, arsenic is mainly present as arseno-lipids, and to a lesser extent, arsenite and methylated As(V) species (Cullen and Reimer, 1989). Arseno-lipids, arseno-sugars, methanoarsenate, dimethylarsenate, and other methylated arsenicals account for 60 to 99% of the arsenic in marine algae and plants (Cullen and Reimer, 1989; Adams *et al.*, 1994). The principal arsenic compounds found in fish and other marine animals are arsenobetaine and arsenocholine (Lawrence *et al.*, 1986; Adams *et al.*, 1994). However, arsenic may also occur in fish tissues as inorganic forms (NRCC, 1978; ATSDR, 1993; CEPA, 1993). The proportion of arsenic in fish tissues that is inorganic has been reported to range from as low as 0.1% to as high as 41%, depending on the species (NRCC, 1978; Vaessen and van Ooik, 1989). It is important from a risk characterization perspective to determine the proportion of inorganic arsenic species that are present in fish as the inorganic forms are the most bioavailable and the most toxic. Complexed organic arsenic species are not readily bioavailable and are more readily eliminated than the inorganic forms. As a result, organic arsenic species are generally considered to be of low toxicity.

Arsenic is present in methylated forms in some terrestrial plants and animals (NRCC, 1978; Nissen and Benson, 1982). Generally, arsenic does not accumulate to high levels in terrestrial plants, as reduced plant growth and other forms of phytotoxicity will occur before arsenic can accumulate to any significant extent (Bennett, 1981). However, some plants are quite tolerant of arsenic in soil (*e.g.*, grapes, corn, carrots, tomatoes, cabbage, tobacco) (Walsh *et al.*, 1977). Furthermore, plant uptake of arsenic is in competition with phosphorus uptake; thus arsenic accumulation is usually restricted as most soils contain greater amounts of phosphorus than arsenic (Adams *et al.*, 1994). On a relative basis, the highest concentrations of arsenic in terrestrial plants tend to occur in plant roots, with intermediate levels occurring in vegetative tissues and the lowest levels in plant reproductive tissues (Walsh *et al.*, 1977).

1.2.5 Food

Due to the extensive cycling of arsenic through biotic and abiotic components of terrestrial and aquatic systems, it is not surprising that arsenic has been detected in most foods consumed by humans. Concentrations of total and/or inorganic arsenic in various Canadian or Ontario foodstuffs are provided in Table 3-4. The chemical form of arsenic in various foodstuffs varies considerably. For example, much of the arsenic in fish is present in a highly complexed form that is not readily bioavailable, or as organoarsenicals (*e.g.*, arsenobetaine, arsenocholine) that are rapidly excreted from the body. Soluble inorganic As(III) and As(V) species are the most bioavailable of the arsenic species and are of primary toxicological concern in humans. Based on limited data, the percentage of arsenic which occurs in an inorganic form in various foods has been reported to typically range from 0 to 1% in saltwater fish, 5% in vegetables, 10 to 15% in freshwater fish, 10% in potatoes, 10% in fruits, 73% in apple juice, 35 to 43% in rice, 49 to 69% in cereals, flour and breads, 15 to 41% in poultry, and as much as 75 to 100% in milk, dairy products, and meats (Pyles and Woolson, 1982; OMOE, 1987; Weiler, 1987; Borum and Abernathy, 1994). Organic forms of arsenic predominate in fish, vegetables and fruits. For a typical mixed diet, approximately 20% of the estimated daily dietary intake of arsenic is inorganic (Borum and Abernathy, 1994). However, a recent study by Yost *et al.*, (1998) suggests that as much as 21 to 40% of the total daily dietary intake of arsenic from a typical mixed diet may be present as inorganic forms.

1.3 Human Exposure Pathways

Soluble inorganic As(III) and As(V) species are the most bioavailable and toxicologically significant arsenic species to humans. Organic arsenic species are rapidly metabolized and eliminated by the body and are generally of low toxicity to humans (Le *et al.*, 1993,1994). Humans may be exposed to inorganic arsenic in ambient air, drinking water, soil, and food. Ingestion of inorganic arsenic in food and drinking water constitute the main exposure pathways for all age classes of the general population (CEPA, 1993; CCME, 1997). United States data indicates that food exposure contributes approximately 92.8% of the total arsenic exposure, while drinking water contributes 7% (Adams *et al.*, 1994). Of the food total arsenic exposure, roughly 90% is attributed to the consumption of seafood, and the remaining 10% to all other foods (Adams *et al.*, 1994). However, most arsenic in seafood is in an organic form, either as arsenobetaine or arsenocholine; thus the contribution to arsenic toxicity from seafood consumption is not directly related to consumption rates alone. A recent study by Yost *et al.*, (1998) suggests that inorganic arsenic may account for 21 to 40% of the total arsenic present in a mixed diet, and that population exposure to inorganic arsenic through the ingestion of food may be greater than previously believed.

Soil and air exposures typically contribute only 0.01 and 0.2% of the total arsenic exposure, respectively (Adams *et al.*, 1994). Canadian data indicates that approximately 0.4 to 3% of the total daily exposure to inorganic arsenic is from soil/dust ingestion for all age classes, with infants and young children incurring as much as 4 to 9% of their total daily intake through this route (CEPA, 1993; CCME, 1997). Inhalation as an exposure route is insignificant for the general population, with the exception of smokers, who may incur as much as 10% of their total daily inorganic arsenic exposure from smoking (CEPA, 1993;

CCME, 1997). Dermal exposure to arsenic *via* direct contact is minor due to the low dermal bioavailability of arsenic (U.S. EPA, 1984).

It should be noted that drinking water exposure varies considerably depending on geological conditions, especially if groundwater is used as the raw drinking water source. High levels of groundwater arsenic have been found to occur in a number of regions where bedrock arsenic content is elevated (*e.g.*, Boyle *et al.*,1969; Brooks *et al.*, 1982; Bottomley, 1984; Meranger *et al.*, 1984).

The estimated typical Canadian daily intake of arsenic from all exposure routes is presented below in Section 2.2. Estimated daily intakes for individuals living in the vicinity of point sources of arsenic contamination, such as mines and/or smelters, are presented in Section 4.1.

1.4 Bioavailability from Exposure Routes

Generally, the water-soluble inorganic As(III) and As(V) species are the most bioavailable. As much as 95% of soluble inorganic arsenic may be absorbed in human gastrointestinal tracts following ingestion (Ray-Bettley, and O'Shea, 1975). Other studies which orally exposed humans and laboratory animals to a variety of inorganic and organic arsenic species (of varying solubility), under varying conditions of exposure, observed oral bioavailability to range from 0 to 99.7% (Hrudey *et al.*, 1996). With respect to the inhalation route, the predominant arsenic species in air (As_2O_3), is almost completely cleared by the lungs, based on rat and hamster studies (Inamusu *et al.*, 1982; Pershagen *et al.*, 1982). A number of other studies, using different inorganic and organic arsenic species, exposure routes and durations, in humans and laboratory animals, found inhalation bioavailability to range from 47 to 92% (Hrudey *et al.*, 1996). In general, oral and inhalation bioavailability varies widely depending on the chemical species, its water solubility, and physiological characteristics of the digestive and respiratory systems. The dermal bioavailability of arsenic is low. Wester *et al.*, (1993) reported that dermal absorption of arsenic in monkeys from soil ranged from 3.2 to 4.5%, while absorption in water ranged from 2 to 6.4%. Only 0.8 to 1.9% of inorganic arsenic, in soil and water respectively, was found to penetrate human skin *in vitro* (Wester *et al.*, 1993).

A number of recent studies have found that the oral bioavailability of arsenic is considerably reduced when administered in a soil or dust matrix, relative to gavage, drinking water or diet administration of soluble inorganic arsenic species. Freeman *et al.*, (1995) reported mean absolute percentage oral bioavailability values of 68, 19, and 14 % for gavage, house dust and soil administration, respectively, in female Cynomolgus monkeys given a single oral dose of 0.62 mg/kg body weight/day (gel capsules containing soil), 0.26 mg/kg body weight/day (gel capsules containing house dust), and 0.62 mg/kg body weight/day as soluble sodium arsenate (gavage). The percentage bioavailability values were based on urinary excretion data and were normalized to 100% As recovery following intravenous administration. An earlier study by Groen *et al.*, (1993) calculated an oral inorganic arsenic bioavailability of 8.3 (±2)%, based on urinary excretion data from dogs administered arsenic in a soil matrix. The results of these 2 studies underscore the importance of accounting for differences in arsenic bioavailability in different media when assessing potential environmental exposures.

1.5 Indices of Chronic Human Arsenic Exposure

Indices of chronic human arsenic exposure include measurements of the arsenic content of hair, urine, blood, and nails. Blood is not generally considered a reliable index as arsenic is rapidly cleared from the blood, with little remaining after 10 hours (Mealy *et al.*, 1959). Blood analysis is therefore of little value in assessing human arsenic exposure and intoxication, except perhaps in the identification of arsenic as a cause of acute poisoning (Hindmarsh and McCurdy, 1986).

Urine analysis is considered a reliable index of recent (*i.e.*, 1 to 3 days) exposure only, due to the rapid and efficient excretion of arsenic in the urine (Hindmarsh and McCurdy, 1986). Analysis of arsenic levels in urine is widely used to assess occupational exposures. As the majority of arsenic elimination by the body occurs through the kidney, urinary arsenic concentrations are generally considered to a be a valid biomarker of exposure. However, for poorly absorbed arsenic compounds, urinary levels will only mirror the amount absorbed and will not reflect the total intake (Gerhardsson and Skerving, 1996). A more detailed discussion of urinary excretion of arsenic, and the application of this indice in estimating arsenic exposures, is available in Part 4, Section 2 of this report.

Data on arsenic concentrations in nails are limited; therefore, nail arsenic concentrations have not been validated as a reliable index of exposure. In addition, it is unclear whether nail arsenic reflects only internal exposure to arsenic, or if it reflects both external and internal exposure (Hindmarsh and McCurdy, 1986). More recently, Gerharrdsson and Skerving (1996) reported that there is a high potential for external contamination of nails, which limits the usefulness of nail analysis in biological exposure monitoring.

Some studies have found that hair arsenic is an unreliable index, due to difficulties in distinguishing internally acquired and externally deposited arsenic, and uncertainties about how arsenic in bloodstream enters hair (Young and Rice, 1944; Hindmarsh and McCurdy, 1986; Gerhardsson and Skerving, 1996). It has been suggested that ingested arsenic may enter hair *via* sweat and/or sebaceous secretions and remain attached to hair for the remainder of that hair's life (Hindmarsh and McCurdy, 1986). Regardless of whether arsenic enters hair from the bloodstream or is deposited from the surrounding atmosphere, it tends to accumulate mostly on the outer surface of a hair. Although a number of studies have shown no clear relationship between hair arsenic levels and severity of toxicity (based on clinical manifestation), and environmental arsenic exposure, it has been concluded by some authors that hair arsenic levels can be reliably used as approximate indicators of chronic exposure and toxicity, providing that external arsenic contamination can be largely excluded (Hindmarsh *et al.*, 1977; Hindmarsh and McCurdy, 1986). To date, exposure levels resulting in measurable increases in hair arsenic have not been defined, and there are presently no available critical limit values for arsenic (and other trace elements) in hair (Wilhelm and Idel, 1996). Therefore, hair analysis is considered by some to be suitable only as a screening tool for large populations where there is continuous exposure to arsenic *via* food and water (Gerhardsson and Skerving, 1996; Wilhelm and Idel, 1996).

It should be noted that a number of factors can confound estimates of arsenic exposure, making it difficult to attribute particular sources of arsenic contamination to measured arsenic concentrations in human tissues or fluids. Key confounding variables reported in the literature include: age, seafood consumption, geographic region, tobacco smoking, drinking, occupation, and sex (Polissar *et al.*, 1990; Arbouine and Wilson, 1992; Bencko, 1995; Gebel *et al.*, 1998). In particular, age and seafood consumption tend to correlate positively with urinary arsenic levels (Gebel *et al.*, 1998).

2.0 BACKGROUND ARSENIC EXPOSURE IN ONTARIO AND/OR CANADA

Tables 3-1 through 3-5 presents Ontario and/or Canadian ambient (or background) arsenic concentrations for aquatic media (*i.e.*, surface water, sediments, groundwater, aquatic biota), soil and dusts, air and terrestrial biota, a variety of Canadian foodstuffs, and human tissues and fluids. Where Ontario-specific data are unavailable, ambient concentrations from other locations in Canada (or other countries) are presented.

Table 3-1 Ontario and Canadian Background Arsenic Concentrations in Aquatic Media

Environmental Medium	Location	Description	Concentration	References
Fresh surface water	Great Lakes	non-point source	< 1.0 µg/L	OMOE, 1996
	Great Lakes	areas of concern (*e.g.*, Bay of Quinte)	2 to 15 µg/L	OMOE, 1996; Jaagumagi and Persaud, 1992
	Ontario rivers		generally not detected (< 1.0 µg/L)	OMOE, 1996
	Lake Superior	47 water samples	range: <0.1 to 1.0 µg/L mean: 0.23 µg/L	Traversy *et al.*, 1975
	Lake Huron	91 water samples	range: 0.1 to 0.8 µg/L mean: 0.44 µg/L	Traversy *et al.*, 1975
	Georgian Bay	64 water samples	range: <0.1 to 0.7 µg/L mean: 0.35 µg/L	Traversy *et al.*, 1975
	Lake Erie	17 water samples	range: <0.1 to 0.6 µg/L mean: 0.25 µg/L	Traversy *et al.*, 1975
	Lake Ontario	24 water samples	range: 0.6 to 1.2 µg/L mean: 0.91 µg/L	Traversy *et al.*, 1975
	Great Lakes Basin Rivers	108 water samples	range: <0.1 to 1.4 µg/L mean: 0.26 µg/L	Traversy *et al.*, 1975
	St. Mary's River	160 water samples	range: <0.1 to 1.0 µg/L mean: 0.37 µg/L	Traversy *et al.*, 1975
	St. Lawrence River	132 water samples	range: <0.1 to 1.0 µg/L mean: 0.61 µg/L	Traversy *et al.*, 1975
	Central Canada	428 surface water samples	<1.0 µg/L[a]	NAQUADAT, 1985

Table 3-1 Ontario and Canadian Background Arsenic Concentrations in Aquatic Media

Environmental Medium	Location	Description	Concentration	References
Precipitation	Various locations	53 rainwater samples throughout Great Lakes Basin	range: <0.1 to 2.5 µg/L mean: 0.72 µg/L	Traversy *et al.*, 1975
	Toronto, Etobicoke, Oakville, North York, Kingston, Ont.	fresh snow samples (particulate matter); filtered snow samples from 1983-84	fresh snow range: 10 to 50 µg/L filtered snow range: 15 to 50 µg/L	Brzezinska-Paudyn *et al.*, 1986
Sediments[b]	Lake Superior	15 sediment samples	range: 0.5 to 8.0 mg/kg mean: 2.03 mg/kg	Traversy *et al.*, 1975
	Lake Huron	10 sediment samples	range: 0.8 to 4.5 mg/kg mean: 2.33 mg/kg	Traversy *et al.*, 1975
	Lake Erie	10 sediment samples	range: 2.0 to 5.5 mg/kg mean: 3.2 mg/kg	Traversy *et al.*, 1975
	Lake Ontario	8 sediment samples	range: 1.5 to 14 mg/kg mean: 4.1 mg/kg	Traversy *et al.*, 1975
	Lake Superior	north shore surficial sediments	<20 mg/kg	Friske, 1985
	Ontario lakes	14 lakes sampled in Ontario	<20 mg/kg	Johnson, 1987
Fish (freshwater)	Lake Erie	31 fish sampled	range: 0.03 to 0.12 mg/kg ww mean: 0.07 mg/kg ww	Traversy *et al.*, 1975
	Lake Ontario	12 fish sampled	range: 0.04 to 0.1 mg/kg ww mean: 0.07 mg/kg ww	Traversy *et al.*, 1975
	remote areas	uncontaminated water bodies	typical range: <0.1 to 0.4 mg/kg ww	Moore and Ramamoorthy, 1984
Aquatic Plants	remote areas	uncontaminated water bodies	typical: <10 mg/kg dry weight	Moore and Ramamoorthy, 1984

Table 3-1 Ontario and Canadian Background Arsenic Concentrations in Aquatic Media

Environmental Medium	Location	Description	Concentration	References
Drinking water	Ontario	from DWSP reports on municipal drinking water from surface and ground water sources	majority below detection (< 1.0 µg/L	OMOE, 1996
	Madoc, Ontario	municipal wells	usually about 3 µg/L, one time maximum of 50 µg/L	OMOE, 1996
	Canada	Ontario drinking water supplies	<5 µg/L	Subramanian and Meranger, 1984; OMOE, 1989
	Canada	domestic and imported bottled water samples from across Canada	range: <1 to 48 µg/L mean: 3 µg/L	Dabeka *et al.*, 1992
Groundwater	Southeastern Ontario	survey of shallow groundwater supplies	<50 µg/L	Michel, 1990

[a] Detection limit was 1.0 µg/L; only one sample from Quebec (2 µg/L) was greater than detection limit.

[b] All sediment samples analyzed for arsenic were surficial (*i.e.*, ≤3 cm depth).

Table 3-2 Ontario and Canadian Background Arsenic Concentrations in Soil and Dusts

Environmental Medium	Location	Description	Concentration	References
Soil	Ontario	typical range surface soil concentrations	14 mg/kg (agricultural land use) 17 mg/kg (all other land uses)	OMOE, 1997
	Ontario	rural	6.3 mg/kg	Frank *et al.*, 1976
	Ontario	agricultural soil	range: 1 to 29 mg/kg average: 6 mg/kg	Kabata-Pendias and Pendias, 1992
	Canada	uncontaminated soils across Canada	range: 4.8 to 13.6 mg/kg <10 mg/kg (average urban and agricultural concentrations)[a]	Kabata-Pendias and Pendias, 1992 Environment Canada, 1996

Table 3-2 Ontario and Canadian Background Arsenic Concentrations in Soil and Dusts

Environmental Medium	Location	Description	Concentration	References
	Ontario	Ontario typical range for non-polluted surface soils; 98th %ILEs	11 mg/kg (rural parkland) 17 mg/kg (old urban parkland)	OMOEE, 1993
	Ontario	uncontaminated agricultural soils	range: 1.1 to 16.7 mg/kg	Frank *et al.*, 1976
	South-western Ontario	untreated agricultural soils	range: 1.1 to 8.6 mg/kg	Miles, 1968
	Canada	uncontaminated soil	<15 mg/kg usually average: 7 mg/kg	NRCC, 1978
	Ontario	uncontaminated soils	range: 1.1 to 8.6 mg/kg	Walsh and Keeney, 1975
Outdoor dusts	Halifax, Nova Scotia	street dusts; 2 samples	range: 5.9 to 8.9 mg/kg	Fergusson and Ryan, 1984

[a] Environment Canada (1996) reports that most urban and agricultural soil concentrations are in 4 to 6 mg/kg range.

Table 3-3 Ontario and Canadian Background Arsenic Concentrations in Air and Terrestrial Biota

Environmental Medium	Location	Description	Concentration	References
Outdoor air	Ontario	rural, 1991 data	mean: 0.001, maximum 0.0019 µg/m^3	OMOE, 1996
	Ontario	urban, 1992 data	mean: 0.003, maximum 0.013 µg/m^3	OMOE, 1996
	Canada	major urban centres	mean: 0.001 µg/m^3 (in PM10)	CCME, 1997
	Canada	major urban centres (1983-1984 data)	range: <0.003 to 0.013 µg/m^3	EAG Ltd., 1984
	Windsor, Ontario	1987-1988 air data	range: 0.001 to 0.004 µg/m^3	Environment Canada, 1988

Table 3-3 Ontario and Canadian Background Arsenic Concentrations in Air and Terrestrial Biota

Environmental Medium	Location	Description	Concentration	References
	Canada	11 Canadian cities and one rural location (1985-1990 data)	range: <0.0005 to 0.017 µg/m^3 (24 h average) mean: 0.001 µg/m^3 (most cities)	Dann, 1990; Environment Canada, 1990
	Toronto, Ont. area	arsenic concentration of airborne particulates from 1982-84	range: 0.04 to 0.15 µg/m^3 mean: 0.08 µg/m^3	Brzezinska - Paudyn *et al.*, 1986
	North America	typical ranges for urban and rural areas	urban range: 0.002 to 0.22 µg/m^3 rural range: 0.001 to 0.007 µg/m^3	Schroeder, 1982
Terrestrial biota *Sphagnum fuscum* moss	Canada	various sites in Canada, including 8 Ontario locations	range: <0.06 to 2.0 mg/kg dry weight	Glooschenko and Arafat, 1988

Table 3-4 Typical Total Arsenic Concentrations in Canadian Foods

Food Type	Location	Description	Concentration (mg/kg ww)	Reference
Fish and seafood				
marine fish	Canada	marine fish sold for human consumption	range: 0.4 to 118	DNHW, 1983
fish (saltwater)	Ontario	total arsenic concentrations and % inorganic	1.1 to 4 (1% inorganic) average: 2.55	OMOE, 1987[a]
fish (freshwater)	Ontario	total arsenic concentrations and % inorganic	0.14 (15% inorganic)	OMOE, 1987[a]
shrimp	Ontario	total arsenic concentrations and % inorganic	0.65 (16% inorganic)	OMOE, 1987[a]
saltwater fish	Canada	typical total arsenic concentrations from 6 Canadian cities	range: 1.85-4.83 mean: 3.05	Dabeka *et al.*, 1993

Table 3-4 Typical Total Arsenic Concentrations in Canadian Foods

Food Type	Location	Description	Concentration (mg/kg ww)	Reference
freshwater fish	Canada	typical total arsenic concentrations from 6 Canadian cities	range: 0.077-1.35 mean: 0.45	Dabeka *et al.*, 1993
shellfish	Canada	typical total arsenic concentrations from 6 Canadian cities	range: 1.01-4.2 mean: 2.04	Dabeka *et al.*, 1993
Meat / poultry products				
meat / poultry	Canada	sold for human consumption	range: nondetect to 0.44	DNHW, 1983
red meat	Ontario	total arsenic concentrations and % inorganic	0.013 to 0.026 (100% inorganic)	OMOE, 1987[a]
poultry	Ontario	total arsenic concentrations and % inorganic	0.021 to 0.023 (41% inorganic)	OMOE, 1987[a]
meat	Canada	typical total arsenic concentrations from 6 Canadian cities	range: <0.001-0.536 mean: 0.024	Dabeka *et al.*, 1993
poultry	Canada	typical total arsenic concentrations from 6 Canadian cities	range: 0.014-0.1 mean: 0.04	Dabeka *et al.*, 1993
organ and muscle meat of sheep, cattle, swine	U.S.	liver, kidney and muscle concentrations	liver: 0.02 to 0.19 kidney: 0.02 to 0.15 muscle: 0.01 to 0.11	Doyle and Spaulding, 1978
chicken	U.S.	liver, kidney and muscle concentrations	liver: 0.70 kidney: 0.28 muscle: 0.09	Doyle and Spaulding, 1978
meats	Canada	food purchased in Ottawa-Hull area	0.05	Smith, 1971
Milk and dairy products				
vanilla ice cream	Ontario	total arsenic concentrations and % inorganic	0.016 (26% inorganic)	OMOE, 1987[a]
milk and dairy products	Canada	typical total arsenic concentrations from 6 Canadian cities	range: 0.0004-0.026 mean: 0.004	Dabeka *et al.*, 1993

Table 3-4 Typical Total Arsenic Concentrations in Canadian Foods

Food Type	Location	Description	Concentration (mg/kg ww)	Reference
ice cream	Canada	typical total arsenic concentrations from 6 Canadian cities	range: 0.0007-0.01 mean: 0.005	Dabeka *et al.*, 1993
dairy	Canada	food purchased in Ottawa-Hull area	0.02	Smith, 1971
Rice				
cooked rice	Ontario	total arsenic concentrations and % inorganic	0.23 to 0.24 (43% inorganic)	OMOE, 1987[a]
cooked rice	Canada	typical total arsenic concentrations from 6 Canadian cities	range: 0.075-0.365 mean: 0.097	Dabeka *et al.*, 1993
Cereals, grains and baked goods				
cereals	Ontario	total arsenic concentrations and % inorganic	0.23 to 0.3 (49% inorganic)	OMOE, 1987[a]
bread	Ontario	total arsenic concentrations and % inorganic	average: 0.024 (50% inorganic)	OMOE, 1987[a]
pastry flour	Ontario	total arsenic concentrations and % inorganic	0.011 (69% inorganic)	OMOE, 1987[a]
cereals and baked goods	Canada	typical total arsenic concentrations from 6 Canadian cities	range: <0.0001-0.142 mean: 0.01	Dabeka *et al.*, 1993
cereals	Canada	food purchased in Ottawa-Hull area	0.05	Smith, 1971
Fruits and fruit juices				
apple juice	Ontario	total arsenic concentrations and % inorganic	0.012 (73% inorganic)	OMOE, 1987[a]
fruits and fruit juices	Canada	typical total arsenic concentrations from 6 Canadian cities	range: <0.0001-0.037 mean: 0.004	Dabeka *et al.*, 1993
garden fruits	Canada	food purchased in Ottawa-Hull area	0.02	Smith, 1971
fruits	Canada	food purchased in Ottawa-Hull area	<0.1	Smith, 1971

Table 3-4 Typical Total Arsenic Concentrations in Canadian Foods

Food Type	Location	Description	Concentration (mg/kg ww)	Reference
Root vegetables				
root vegetables	Canada	food purchased in Ottawa-Hull area	<0.02	Smith, 1971
potatoes	Canada	typical total arsenic concentrations from 6 Canadian cities	range: <0.0001-0.044 mean: 0.0098	Dabeka *et al.*, 1993
potatoes	Canada	food purchased in Ottawa-Hull area	<0.1	Smith, 1971
Other vegetables				
vegetables (including potato products)	Canada	typical total arsenic concentrations from 6 Canadian cities	range: <0.0001-0.084 mean: 0.007	Dabeka *et al.*, 1993
leafy vegetables	Canada	food purchased in Ottawa-Hull area	<0.1	Smith, 1971
legumes	Canada	food purchased in Ottawa-Hull area	<0.02	Smith, 1971
Fats and oils				
fats and oils	Canada	typical total arsenic concentrations from 6 Canadian cities	range: <0.0001 to 0.057 mean: 0.02	Dabeka *et al.*, 1993
Sugars and sweets				
sugar and candies	Canada	typical total arsenic concentrations from 6 Canadian cities	range: 0.001 to 0.105 mean: 0.0096	Dabeka *et al.*, 1993
sugar products	Canada	food purchased in Ottawa-Hull area	0.08	Smith, 1971
Beverages				
beverages	Canada	typical total arsenic concentrations from 6 Canadian cities	range: 0.0004-0.009 mean: 0.003	Dabeka *et al.*, 1993
tea	Ontario	total arsenic concentrations and % inorganic	0.035 (26% inorganic)	OMOE, 1987[a]
drinks	Canada	food purchased in Ottawa-Hull area	0.02	Smith, 1971

Table 3-4 Typical Total Arsenic Concentrations in Canadian Foods

Food Type	Location	Description	Concentration (mg/kg ww)	Reference

[a] All food samples were comprised of one homogenized sample, analyzed in duplicate or triplicate, except for saltwater fish and apple juice. Percent inorganic arsenic was calculated by dividing measured average inorganic concentration in foods by the average measured total arsenic concentration.

[b] All food samples were prepared as for normal consumption and then homogenized.

Table 3-5 Background Arsenic Concentrations in Human Biological Tissues and Fluids

Tissue or Fluid Type	Location	Description	Concentration	References
Hair	Nova Scotia	normal hair concentrations in persons living in uncontaminated areas	<1 µg/g ww	Hindmarsh *et al.*, 1977
	Canada	5- to 9-year-olds in town without a gold-mine	mean: 0.39 µg/g	CPHA, 1978
	U.S.	children in towns without copper smelters	median: 0.08 µg/g	Baker *et al.*, 1977
	not specified	boys living in metropolitan city	mean: 0.15 µg/g	Bencko and Symon, 1977
	not specified	1000 persons examined	<1 µg/g for 80% of subjects average: 0.81 µg/g median: 0.51 µg/g	Smith, 1964
	not specified	no known exposure to arsenic	geometric mean: 0.3 µg/g range: 0.01-0.4 µg/g median: 0.11 µg/g	Leslie and Smith, 1978; Cornelis, 1973
	Glasgow area in Scotland	1200 samples from residents	range: 0.02-8.17 µg/g dw geometric mean: 0.46 µg/g dw	Liebscher and Smith, 1968
	not specified	typical background concentration	0.41 µg/g ww typically <1 µg/g ww	Liebscher and Smith, 1968
Whole blood	U.S.	50 female non-smokers from uncontaminated areas	mean: 1.5 µg/L	Kagey *et al.*, 1977

Table 3-5 Background Arsenic Concentrations in Human Biological Tissues and Fluids

Tissue or Fluid Type	Location	Description	Concentration	References
	not specified	3 samples	mean: 0.002 µg/g ww	Bergström and Wester, 1966
	Denmark	7-16 samples from healthy individuals	mean: 25 µg/L	Heydorn, 1969
	Taiwan	6-17 samples from normal subjects	mean: 21.6 µg/L	Heydorn, 1969
	not specified	8 normal subjects	mean: 0.004 µg/g ww	Brune *et al.*, 1966
Blood	not specified	typical background concentration	0.007 µg/g ww	Liebscher and Smith, 1968; Yamamura and Yamauchi, 1976
	not specified	nonoccupationally exposed individuals	typical range: 1 to 4 µg/L	Bencko and Symon, 1977
	Czechoslovakia	10-year-old children in country town	range: 0.0005-0.0320 µg/g mean: 0.00145 µg/g ww	Bencko and Symon, 1977
	Czechoslovakia	10-year-old children in metropolitan city	range: 0.0005-0.0038 µg/g mean: 0.00188 µg/g ww	Bencko and Symon, 1977
	Czechoslovakia	10-year-old children near coal-fired power plant	range: 0.0025-0.0082 µg/g mean: 0.00453 µg/g ww	Bencko and Symon, 1977
	U.S.	50 female smokers and 49 nonsmokers	smokers: 2.3 µg/L nonsmokers: 1.5 µg/L	Kagey *et al.*, 1977
Red cells	Denmark	7-16 samples from healthy individuals	mean: 2.7 µg/L	Heydorn, 1969
	Taiwan	6-17 samples from normal subjects	mean: 32.7 µg/L	Heydorn, 1969
Plasma	Denmark	7-16 samples from healthy individuals	mean: 2.4 µg/L	Heydorn, 1969
	Taiwan	6-17 samples from normal subjects	mean: 15.4 µg/L	Heydorn, 1969
Serum	not specified	3 samples	mean: 0.0011 µg/g ww	Bergström and Wester, 1966

Table 3-5 Background Arsenic Concentrations in Human Biological Tissues and Fluids

Tissue or Fluid Type	Location	Description	Concentration	References
	not specified	11 samples from normal humans	mean: 1.1 µg/L	Damsgaard *et al.*, 1973
Urine	U.S.	normal level for persons in uncontaminated areas	< 50 µg/L	Landrigan, 1981
	U.S., Washington	comparison group	speciated arsenic 10.1 µg/L	Polissar *et al.*1990
	U.S.	Basal levels without specific exposure to arsenic	5.6 µg/L	Foa *et al.*, 1984
	U.S.	background	speciated arsenic 4 to 8 µg/L	Vahter, 1986
	U.S.	control community	total arsenic 10 to 16.6 µg/L or 17 to 19 µg/g creatinine	Binder *et al.*, 1987
	U.S.	background	speciated arsenic 4.4 µg/L	Farmer and Johnson, 1990
	U.S.	background	speciated arsenic 9.2 to 14.5 µg/L	Kalman *et al.*, 1990
	Great Lakes	communities situated around Great Lakes	not detected (0.05) to 5.2 µg/L	Anderson *et al.*, 1998
	Argentina	control community	total arsenic 7.6 to 13 µg/L	Concha *et al.*, 1998
	Mexico	control community	total arsenic 33 to 182 (mean 74.3) µg/L	Diaz-Barriga *et al.*, 1993
	Mexico	control	speciated arsenic 19.5 µg/L	Del Razo *et al.*, 1997
	Glasgow, U.K.	control population	speciated arsenic adult: 1.2-39.8 (mean 5.8) µg/g creatinine child: 2.5-19.4 (10.2) µg/g creatinine	Johnson and Farmer, 1989
	Belgium	background	4.4 to 24 µg/L	Buchet *et al.*, 1980a, 1981a,b
	Germany	background	speciated arsenic 0.29 to 24 (mean 7.58) µg/24 hour	Gebel *et al.*, 1998

Table 3-5 Background Arsenic Concentrations in Human Biological Tissues and Fluids

Tissue or Fluid Type	Location	Description	Concentration	References
	Germany	control community	total arsenic 0.3 to 89.2 µg/L	Trepka *et al.*, 1996
	Europe	reference concentrations	0.16 to 40 µg/L	Kristiansen *et al.*, 1997
	Europe	normal concentrations	<10 µg/L	Gerhardsson and Skerving, 1996
	Finland	background	speciated arsenic 5 µg/L	Kurttio *et al.*, 1998
	Denmark	background	3.9 to 58 nmol/nmol creatinine	Poulsen *et al.*, 1994
	Sweden	background	speciated arsenic 8 µg/g creatinine	Vahter and Lind, 1986
	Cornwall	control	total arsenic without arsenobetaine 2.5 to 5.3 µg/L	Kavanagh *et al.*, 1998
	not specified	10-year old boys with no known exposure to arsenic	mean: 11 µg/L	Bencko and Symon, 1977
	not specified	groups of children living within 7.5 km of coal-fired power plant	mean: 18.9-25.3 µg/L range: <1-105 µg/L	Bencko and Symon, 1977
	not specified	preemployment examinations of over 200 men	background level: 53 µg/L	Pinto *et al.*, 1976
	not specified	41 unexposed workers	geometric mean: 21 µg/L	Smith *et al.*, 1977
	not specified	women living over 70 km from smelter	mean: 30 µg/L	Holmqvist, 1975
	not specified	total arsenic in urine of 4 subjects	10-30 µg/L	Braman and Foreback, 1973
	not specified	smelter workers without arsenic exposure	total arsenic average: 40 µg/L	Lundgren, 1954
	World-wide	expected range of values in an ostensibly unexposed population	total arsenic <100 µg/L	WHO, 1980

Table 3-5 Background Arsenic Concentrations in Human Biological Tissues and Fluids

Tissue or Fluid Type	Location	Description	Concentration	References
	U.S.	children in 3 control towns (no copper smelter present)	geometric mean: 6 µg/L	Baker *et al.*, 1977
	U.S.	upper limit of background or normal concentrations	20 µg/L	ATSDR, 1993
Nails	not specified	normal levels based on neutron activation analytical method	approximately 0.28 ppm	Liebscher and Smith, 1968
Muscle	not specified	typical background concentration	0.013 µg/g ww	Liebscher and Smith, 1968
Bone	not specified	typical background concentration	0.047 µg/g ww	Liebscher and Smith, 1968
Skin	not specified	typical background concentration	0.034 µg/g ww	Liebscher and Smith, 1968
Liver	not specified	typical background concentration	0.008 µg/g ww	Liebscher and Smith, 1968
Lungs	not specified	typical background concentration	0.021 µg/g ww	Liebscher and Smith, 1968
Total body content	not specified	typical background concentration	approximately 1 µg	Liebscher and Smith, 1968

2.1 Estimated Canadian Daily Dietary Intake of Arsenic

Utilizing age and sex-specific food consumption rate data for 112 food categories representative of the Canadian diet, Yost *et al.*, (1998) took the percentage of inorganic arsenic in the foods analyzed by OMOE (1987) and multiplied by the corresponding food concentrations reported by Dabeka *et al.*, (1993) to estimate total Canadian dietary intake of inorganic arsenic for 3 age/sex classes: (children ages 1 to4; women ages 20 to 39; men ages 20 to 39). Consumption data were provided by the Nutrition Canada Survey of Department of Health and Welfare, Canada (Yost *et al.*, 1998). The total daily dietary intake of inorganic arsenic for these 3 classes was 4.8, 8.1, and 12.7 µg/day, respectively (Yost *et al.*, 1998). The average daily intake for all classes combined was 8.3 µg/day. Based on their analysis of the OMOE (1987) data, the authors concluded that as much as 21 to 40% of total dietary arsenic is present as the soluble inorganic forms. This suggests that dietary intake of inorganic arsenic may be higher than previously believed (Yost *et al.*, 1998).

Dabeka *et al.* (1993) had previously estimated daily Canadian dietary intakes for total arsenic, averaged over 6 Canadian cities, to range from 14.9 µg/day (F and M children aged 1 to 4), 29.9 µg/day (F and M children aged 5 to 11), 31.7 and 40.9 µg/day (12 to 19 yr old F and M, respectively), 34.1 and 59.2 µg/day (20 to 39 yr old F and M, respectively), 52.8 and 43 µg/day (40 to 65 yr old F and M, respectively), and 25.8 and 35.7 µg/day (>65 yr old F and M, respectively). The overall average estimated daily dietary intake for the entire Canadian population was 38.1 µg/day. An earlier estimate of daily arsenic intake from food was reported to range from 2.6 to 101 µg/day for total arsenic in adults, with an average intake of 16.7 µg/day (Dabeka *et al.*, 1987). However, this study was based on limited data and only estimated daily arsenic intake for male and female adults. The data from Dabeka *et al.* (1987) as well as 1980's or earlier data from other countries, was previously used to estimate the daily intake of inorganic arsenic from food (GCDWQ, 1996); a dietary EDI of approximately 10.5 µg/day was estimated. Despite the limitations of the data used to derive this estimate, it is in agreement with the average daily inorganic arsenic intake for all age classes recently estimated by Yost *et al.* (1998) to be 8.3 µg/day. The estimated chronic daily intake of 11 µg/day from a typical Ontario background diet (Fleming and Kuja, 1998) is also in close agreement with the estimates of Yost *et al.* (1998), and GCDWQ (1996).

2.2 Estimated Average Total Daily Intake of Inorganic Arsenic by Canadians

The total average daily intake of inorganic arsenic by Canadians from all environmental sources (uncontaminated areas) was estimated to range from 0.1 to 2.6 µg/kg body weight/day, with the greatest exposure occurring in infants and young children (CEPA, 1993). The total EDI values, in µg/kg body weight/day for all age classes assessed in CEPA (1993) were 0.1 to 2.6 (0 to 5 yrs); 0.3 to 2.4 (0.5 to 4 yrs); 0.2 to 2.1 (5 to 11 yrs); 0.1 to 1.3 (12 to 19 yrs); and 0.1 to 0.7 (20 to 70 yrs). Cigarette smoking was estimated to contribute an additional 0.01 to 0.04 µg/kg body weight/day in adolescents and adults (CEPA, 1993). It should be noted that these estimates were based on environmental data collected before 1991, and the assumption that 37% of the arsenic content of foods was inorganic. Thus, these estimates may change slightly if the recent daily Canadian dietary intakes of inorganic arsenic and estimates of inorganic arsenic content from Yost *et al.*, (1998) as well as environmental concentrations specific to Ontario, were to be incorporated into the calculations used in CEPA (1993).

The OMOE (1996) examined the relative contribution of various pathways of exposure to total daily intake of inorganic arsenic *via* ingestion, and estimated a daily intake of 13.1 µg/d (1 and 0.2 µg/kg bw/d for a child and adult, respectively), most of which was contributed by food (84%) and drinking water (15%). Soil/dust ingestion pathways contributed less than 1% to the total.

3.0 MINE AND SMELTER ARSENIC EXPOSURE ISSUES

In general, the material described in Section 1.0 also applies to human exposure scenarios in the vicinity of mines and/or smelters. However, there are a number of key differences between exposure to background arsenic concentrations from multiple environmental sources, and exposure to arsenic from a point source, such as a mine or smelter, which are briefly discussed below.

3.1 Arsenic Emissions From Mining/Smelting Operations

Base-metal and gold mines and smelting operations are the principal anthropogenic source of arsenic released to the Canadian environment. Based on 1988 emissions data, the annual amount of arsenic released to water, air, and land by base-metal production activities is approximately 15, 310, and 770 tonnes, respectively (MacLatchy, 1992). Gold-milling operations and gold ore roasters discharge significant amounts of arsenic in their liquid effluents and air emissions. Weathering of waste rock and tailings also releases significant amounts of arsenic into the environment, especially at abandoned base and precious metal mine sites where no leachate treatment systems are in place (Errington and Ferguson, 1987). The mining, smelting, milling, and roasting of base and precious metals account for the majority of As_2O_3 present in the atmosphere.

3.2 Major Human Exposure Pathways in Vicinity of Mines/Smelters

The greatest difference between ambient arsenic exposure and exposure to arsenic in the vicinity of mining and smelting activities is that exposure levels are often much higher near mines, smelters, and associated metal production operations (*e.g.*, mills, roasters). Section 4.0 presents information on the magnitude of exposure to arsenic in various media in the vicinity of mining and/or smelting activities.

In CEPA (1993), estimates of daily inorganic arsenic intake for Canadians living near point sources of contamination (including but not limited to mines and smelters), indicate that ingestion of food and drinking water is the major exposure pathway, similar to the ambient exposure scenario. While food ingestion estimates are roughly equal to those in the ambient scenario, estimates of the exposure contribution from drinking water are considerably higher; up to 100-fold greater than ambient exposure estimates. In addition, the soil/dusts ingestion and inhalation contributions to exposure are estimated to be much higher for individuals living near point sources; especially in children and infants (*i.e.*, as much as 2 orders of magnitude above ambient exposure scenario) (CEPA, 1993). It should be noted that these estimates were based on limited point source monitoring data from various geographical locations, and represent a highly unlikely "worst case scenario" in which an individual is exposed to contaminated air, water, and soil (CEPA, 1993). A number of human health risk assessments conducted in areas of mining/smelting activity have generally shown higher contributions to overall human exposure from soil/dust ingestion, ingestion of local foods (*e.g.*, fish, livestock, vegetables), and drinking water due to elevated arsenic concentrations in local air, soil, vegetation (including vegetable gardens and fruit orchards), surface and ground water supplies, compared to areas with no mining/smelting activity. It should be noted

however, that the major exposure pathways can differ across mine/smelter sites, depending on a variety of conditions such as site geology, hydrology, local climate and weather patterns, land use, types of human and ecological receptors present, *etc.* For mine and smelter workers, the predominant exposure pathway is usually inhalation. Estimates of daily inorganic arsenic intake for individuals living near mines or smelters (or other point sources of arsenic contamination) are presented in Section 4.1.

3.3 Arsenic Bioavailability in Vicinity of Mines/Smelters

Recent studies have indicated that arsenic bioavailability from smelter-impacted soils may be less than previously believed. Based on data collected from the Anaconda, Montana smelter site, a number of mineralogic constraints on oral arsenic bioavailability from smelter-impacted soils have been reported (Davis *et al.,* 1996). First, smelter-impacted soils contain relatively insoluble arsenic oxides and phosphates which are poorly absorbed from the gastrointestinal tract. Second, a significant proportion of arsenic in smelter-impacted soils is encapsulated within insoluble matrices (*e.g.*, silica, quartz). Third, arsenic in these mineral complexes is protected from dissolution by rinding due to precipitation or alteration reactions that occur during weathering. Fourth, the dissolution kinetics of arsenic in these matrices as they pass through the gastrointestinal tract are slow (Davis *et al.,* 1996). These findings support the observations of Groen *et al.,* (1993) and Freeman *et al.,* (1995), who found reduced oral bioavailabilities for arsenic administered in soil or dust matrices versus arsenic administered in drinking water, diet or gavage as soluble inorganic forms.

4.0 MAGNITUDE OF ARSENIC EXPOSURE IN VICINITY OF MINING/SMELTING ACTIVITY

Reported arsenic concentrations in the vicinity of mines and/or smelters from various geographic locations are presented in the following tables. Table 3-6 presents arsenic concentrations in aquatic media (*i.e.*, surface water, sediments, groundwater, aquatic biota). Table 3-7 presents concentrations for soils and dusts, Table 3-8 provides data for air and terrestrial biota. Table 3-9 presents arsenic concentrations in some human and animal foods. Arsenic concentrations in human hair and urine are presented in Table 3-10.

Table 3-6 Concentrations of Arsenic in Aquatic Media Located Near Mining/Smelting Activity

Environmental Medium	Location	Description	Concentration	References
Fresh surface water	Moira River watershed	downstream of former gold mine	generally 1 to 50 µg/L, historical maximum values of 390 and 56,000 µg/L	OMOE, 1996
	Moira Lake, Ontario	near abandoned gold mines; 1980s data	mean: 45 µg/L max: 140 µg/L	Diamond, 1990
	Northwest Ontario	creeks and lakes near mining facilities	250 to 12,000 µg/L	OMOE, 1996
	Mitchell Brook, Nova Scotia	near abandoned gold mines; 1980s data	mean: 45 µg/L max: 140 µg/L	Brooks *et al.*, 1982
	Keg and Kam Lakes, Yellowknife	lakes near gold mines and roasters	range: 700-5500 µg/L (1970s) range: 545-645 µg/L (1990s)	Wagemann *et al.*, 1978; Reimer and Bright, 1992
	Silver Creek Mine, Park City, Utah, U.S.	downstream creek samples	range: 5-6 µg/L	ATSDR, 1988
	Murray Smelter, Salt Lake County, Utah, U.S.	creek samples adjacent to, and downstream of smelter	range: 40 to 170 µg/L	ATSDR, 1997
	North West Territories, Yellowknife area	natural water bodies (*i.e.*, lakes, streams, rivers etc.) near gold mining/smelting activity	range: 4 to 12,400 µg/L	CPHA, 1977; Falk *et al.*, 1973

Table 3-6 Concentrations of Arsenic in Aquatic Media Located Near Mining/Smelting Activity

Environmental Medium	Location	Description	Concentration	References
Mining/Smelting Wastewaters	mines and smelters in Yellowknife area and elsewhere in Canada	mine waters, smelter effluents	range: 50 to 19,000 µg/L	Williams, 1975; Falk *et al.*, 1973
	Yellowknife area	mine tailings suspended in water	range: 2500 to 4000 mg/L (as total As)	Berube *et al.*, 1973
Precipitation	North West Territories, Yellowknife area	snow samples	range: 2.8 to 460 µg/L	Hardin, 1975
	North West Territories, Yellowknife area	melted snow samples	range: 70 to 160 µg/L	Prokopuk, 1976
Freshwater sediments	Flin Flon, Man.; Sudbury, Ont.; Atlantic Canada	near base and precious metal mining and ore processing operations	average levels: 100-200 mg/kg max: 650 mg/kg	Bailey, 1988; Palmer *et al.*, 1989; Franzin, 1984
	Shubenacadie watershed, NS; Moira Lake, Ont.; Yellowknife, NWT	near gold mines and an abandoned precious metal refinery	range of means: 700-5000 mg/kg max: 18,650 mg/kg	Trip and Skilton, 1985; Diamond, 1990; Reimer and Bright, 1992; Sutherland, 1989
	Murray Smelter, Salt Lake County, Utah, U.S.	creek sediments downstream from smelter	214 mg/kg (single sample)	ATSDR, 1997
Marine/estuarine sediments	near Tacoma, Washington	Puget Sound sediments near smelter	max: 10,000 mg/kg	Woolson, 1977
Tap water	San Luis Potosi, Mexico	urban area near smelter urban area 7 km from smelter	range: 9.9 to 17.6 µg/L mean: 13.7 µg/L range: 15.5 to 20.9 µg/L mean: 17.5 µg/L	Díaz-Barriga *et al.*, 1993

Table 3-6 Concentrations of Arsenic in Aquatic Media Located Near Mining/Smelting Activity

Environmental Medium	Location	Description	Concentration	References
	Ajo, Arizona, U.S.	within 2 miles of copper mine and smelter	mean: 90 µg/L	Morse *et al.*, 1979
	Anaconda smelter site, Montana	vicinity of smelter	range: <4 to 32 µg/L	ATSDR, 1987
	Yellowknife, NWT	drinking water near gold smelter	range: <10 to 740 µg/L	de Villiers and Baker, 1969; CPHA, 1977
Groundwater/ Well water	Northern Ontario		occasional exceedence of ODWO (25 µg/L), maximum of >1000 µg/L	OMOE, 1996
	Big River Mine, Missouri, U.S.	samples from several wells and springs	range (total): nd to 110 µg/L range: (dissolved): nd to 51 µg/L	ATSDR, 1996
	Murray Smelter, Salt Lake County, Utah, U.S.	groundwater in vicinity of smelter; not used for drinking water	range: <0.009 mg/L to 166 mg/L	ATSDR, 1997
	Waverley, Nova Scotia	well water used for drinking in area of former gold mining activity	60 to 140 µg/L	Hindmarsh *et al.*, 1977
	Anaconda smelter site, Montana	vicinity of smelter; two samples from hand dug wells	range: 57 to 72 µg/L	ATSDR, 1987
Freshwater fish	Yellowknife; Halifax County, NS; Moira Lake, Ont.	fish sampled near active and abandoned gold mining operations	range of maximum concentrations: 2.36 to 4.77 mg/kg ww	Gemmill, 1977; Azcue, 1992, Dale and Freedman, 1982

Table 3-6 Concentrations of Arsenic in Aquatic Media Located Near Mining/Smelting Activity

Environmental Medium	Location	Description	Concentration	References
Aquatic plants	Nova Scotia; Manitoba; Yellowknife, NWT	plants sampled in vicinity of gold mining operations	range: 206 to 4900 mg/kg dry weight	Dale and Freedman, 1982; Franzin and MacFarlane, 1980; Wagemann *et al.*, 1978; Reimer and Bright, 1992
Zooplankton	Keg Lake, Yellowknife, NWT	sampled near gold mining operations; 1970s data	mean: 1875 mg/kg dry weight max: 2400 mg/kg dry weight	Wagemann *et al.*, 1978

nd non-detectable

Table 3-7 Arsenic Concentrations in Soils and Dusts in Vicinity of Mining/Smelting Activity

Environmental Medium	Location	Description	Concentration	References
Soil	Ontario	near historical gold roasting facilities	15 to 1000 mg/kg	OMOE, 1996
	Ontario	near iron ore sintering facilities	<1400 mg/kg	OMOE, 1996
	Ontario	near secondary lead smelting facilities	6 to 283, maximum of 2000 mg/kg	OMOE, 1996
	Ontario	mine tailings	most <2000 mg/kg, maximum 4%	OMOE, 1996
	Balmertown, Ontario	community exposed to contaminated mine tailings near Placer Domes Campbell mine	range: 30 to 800 mg/kg	Fleming and Kuja, 1998
	various locations in Canada	near base-metal smelters and gold-mining and roasting operations	range of means: 50-110 mg/kg max: >10,000 mg/kg	CEPA, 1993

Table 3-7 Arsenic Concentrations in Soils and Dusts in Vicinity of Mining/Smelting Activity

Environmental Medium	Location	Description	Concentration	References
	Ontario and Nova Scotia	soils near base and precious metal mine tailings	typical range: 3000-4000 mg/kg max: 75,000 mg/kg	Hawley, 1980; Dale and Freedman, 1982
	Silver Creek Mine, Park City, Utah, U.S.	soil/tailings mixture	range: 12 to 400 mg/kg	ATSDR, 1988
	Tacoma, Washington, U.S.	median of 0.3 miles from copper smelter median of 6.3 miles from copper smelter	mean: 352.5 mg/kg mean: 29.6 mg/kg	Polissar *et al.*, 1990
	Murray Smelter, Salt Lake County, Utah, U.S.	residential areas in vicinity of smelter	range: 41 to 470 mg/kg mean: 206 mg/kg	ATSDR, 1997
	Northern Palatinate Region of Germany	areas of high As ores and former mining activity	range: 76 to 592 mg/kg	Gebel *et al.*, 1998
	San Luis Potosi, Mexico	urban area near smelter urban area 7 km from smelter	range: 117 to 1396 mg/kg mean: 421.6 mg/kg range: 5.7 to 18 mg/kg mean: 10.2 mg/kg	Díaz-Barriga *et al.*, 1993
	near Tacoma, Washington, U.S.	within 10 km vicinity of copper smelter	range: <1 to 380 mg/kg	Crecelius *et al.*, 1974
	ASARCO smelter, Tacoma, Washington	within 0.3 km of smelter	range: 20 to 1940 mg/kg mean: 421 mg/kg	Lee and Kissel, 1995
	Cornwall, UK	areas of historical tin, copper and arsenic mining	range: 144 to 892 mg/kg mean: 322 mg/kg	Xu and Thornton, 1985

Table 3-7 Arsenic Concentrations in Soils and Dusts in Vicinity of Mining/Smelting Activity

Environmental Medium	Location	Description	Concentration	References
	Cornwall, Derbyshire, Shipham, Somerset, UK	topsoil beneath pasture herbage consumed by livestock in regions of historical mining and smelting activity	range: 5.97 to 925 mg/kg	Li and Thornton, 1993
	Devon and Cornwall, UK	near areas of past intense mining and smelting of arsenical ores	no mine waste range: 120 to 1695 mg/kg mean: 365 mg/kg containing mine waste range: 345 to 52,600 mg/kg mean: 4499 mg/kg	Kavanagh *et al.*, 1998
	Anaconda, Montana	former copper smelter area: perimeter, bare, hardpack, garden area and sandbox soil samples	range of geometric means for soil sample types: 121 to 236 mg/kg	Hwang *et al.*, 1996
	Mill Creek, Anaconda, and Opportunity, Montana	towns adjacent to (and downwind of), upwind of, and 6 km downwind of former copper smelter site, respectively	range: 16 to 1950 mg/kg	Binder *et al.*, 1987
Outdoor dusts	San Luis Potosi, Mexico	urban area near smelter (window sill) urban area 7 km from smelter (window sill)	range: 514 to 2625 mg/kg mean: 979.3 mg/kg range: 17.5 to 39 mg/kg mean: 26 mg./kg	Diaz-Barriga *et al.*, 1993
Indoor dusts	Silver Creek Mine, Park City, Utah, U.S.	dust samples from several residences	range: 0 to 8.8 µg/g	ATSDR, 1988
	Big River Mine, Flat River-Desloges, Missouri, U.S.	home dust samples from vacuum cleaners	range: 1.2 to 13.2 µg/g mean: 5.75 µg/g	ATSDR, 1996

Table 3-7 Arsenic Concentrations in Soils and Dusts in Vicinity of Mining/Smelting Activity

Environmental Medium	Location	Description	Concentration	References
	Tacoma, Washington, U.S.	median of 0.3 miles from copper smelter	mean vacuum bag concentration: 375 µg/g mean surface dust concentration: 27 ng/cm^2 mean settled housedust concentration: 3.8 ng/week/cm^2	Polissar *et al.*, 1990
		median of 6.3 miles from copper smelter	mean vacuum bag concentration: 39.6 µg/g mean surface dust concentration: 12.9 ng/cm^2 mean settled housedust concentration: 0.1 ng/week/cm^2	
	Murray Smelter, Salt Lake County, Utah, U.S.	residences within vicinity of smelter	range: <10 µg/g to 94 µg/g mean: 27 µg/g	ATSDR, 1997
	Ajo, Arizona, U.S.	within 2 miles of copper mine and smelter (wood floors of residences)	mean: 342.2 µg/g	Morse *et al.*, 1979
	Devon and Cornwall, UK	homes near areas of past intense mining and smelting of arsenical ores	range: 24 to 3740 µg/g	Kavanagh *et al.*, 1998
	Anaconda, Montana	interior dusts from residences in variety of locations near former copper smelter site	geometric mean: 73 mg/kg	Hwang *et al.*, 1996
	Mill Creek, Anaconda, and Opportunity, Montana	homes in towns adjacent to (and downwind of), upwind of, and 6 km downwind of former copper smelter site, respectively	range: 12 to 386 µg/g	Binder *et al.*, 1987

Table 3-7 Arsenic Concentrations in Soils and Dusts in Vicinity of Mining/Smelting Activity

Environmental Medium	Location	Description	Concentration	References
	Ruston enclave, Washington, near Tacoma smelter	residences within 1 mile of smelter	vacuum cleaner dust range: 330 to 1300 µg/g attic dust 2100 µg/g (one sample from home within 0.4 miles of smelter)	Milham and Strong, 1974

All soil data is based on surficial samples collected within one foot or less of the surface.

Table 3-8 Arsenic Concentrations in Air and Terrestrial Biota in Vicinity of Mining/Smelting Activity

Environmental Medium	Location	Description	Concentration	References
Outdoor air	Ontario	near point sources, 1990-1994 data from 5 facilities	mean: 0.011 µg/m^3, maximum 0.15 µg/m^3	OMOE, 1996
	Utah copper smelter, U.S.	within 80 km radius of a non-ferrous smelter	annual mean: 0.03 µg/m^3	Ball *et al.*, 1983
	Yellowknife	near Giant gold ore roaster; 1980s and early 1990s data	range of annual averages: 0.0086 to 0.3 µg/m^3	CEPA, 1993
	Tacoma, Washington, U.S.	median of 0.3 miles from copper smelter; coarse/fine particulates median of 6.3 miles from copper smelter; coarse/fine particulates	mean: 0.154 / 0.09 µg/m^3 mean: 0.004 /0.004 µg/m^3	Polissar *et al.*, 1990
	San Luis Potosi, Mexico	urban area near smelter urban area 7 km from smelter	range: 0.13 to 1.45 µg/m^3 mean: 0.48 µg/m^3 range: 0.04 to 1.5 µg/m^3 mean: 0.26 µg/m^3	Díaz-Barriga *et al.*, 1993

Table 3-8 Arsenic Concentrations in Air and Terrestrial Biota in Vicinity of Mining/Smelting Activity

Environmental Medium	Location	Description	Concentration	References
	North West Territories	near gold mine; arsenic concentrations in suspended particulate matter	24 hr range: <0.01 to 3.91 µg/m³ annual range: 0.02 to 2.75 µg/m³	Prokopuk, 1976
Indoor air	Tacoma, Washington, U.S.	median of 0.3 miles from copper smelter; coarse/fine particulates	mean: 0.02 / 0.03 µg/m³	Polissar *et al.*, 1990
		median of 6.3 miles from copper smelter; coarse/fine particulates	mean: 0.002 / 0.005 µg/m³	
	ASARCO smelter, Tacoma, Washington	within 0.3 km of smelter	range: 0.00004 to 0.134 µg/m³ mean: 0.017 µg/m³	Lee and Kissel, 1995
Terrestrial biota *Sphagnum fuscum* moss	Canada	samples collected near mining and smelting regions of Flin Flon Man., Thompson, Man., Atikokan, Ont., Rouyn-Noranda, Que.	range: 1.8 to 31 mg/kg dry weight	Glooschenko and Arafat, 1988

All soil data is based on surficial samples collected within one foot or less of the surface.

Table 3-9 Arsenic Content of Some Human and Animal Foods in Areas of Mining/Smelting Activity

Food Type	Location	Description	Concentration (mg/kg ww)	Reference
lettuce	Cornwall, UK	areas of historical mining of tin, copper and arsenic	range: 0.15 to 3.88 mg/kg mean: 0.85 mg/kg	Xu and Thornton, 1985
onion	Cornwall, UK	areas of historical mining of tin, copper and arsenic	range: 0.1 to 0.49 mg/kg mean: 0.2 mg/kg	Xu and Thornton, 1985

Table 3-9 Arsenic Content of Some Human and Animal Foods in Areas of Mining/Smelting Activity

Food Type	Location	Description	Concentration (mg/kg ww)	Reference
beetroot	Cornwall, UK	areas of historical mining of tin, copper and arsenic	range: 0.02 to 0.93 mg/kg mean: 0.17 mg/kg	Xu and Thornton, 1985
carrot	Cornwall, UK	areas of historical mining of tin, copper and arsenic	range: 0.1 to 0.93 mg/kg mean: 0.21 mg/kg	Xu and Thornton, 1985
pea	Cornwall, UK	areas of historical mining of tin, copper and arsenic	range: 0.01 to 0.11 mg/kg mean: 0.04 mg/kg	Xu and Thornton, 1985
bean	Cornwall, UK	areas of historical mining of tin, copper and arsenic	range: 0.02 to 0.09 mg/kg mean: 0.04 mg/kg	Xu and Thornton, 1985
pasture herbage	Cornwall, Derbyshire, Shipham, Somerset, UK	pasture herbage consumed by livestock in regions of historical mining and smelting activity	range: 0.03 to 4.86 mg/kg	Li and Thornton, 1993

Table 3-10 Arsenic Concentrations in Human Biological Tissues and Fluids from Individuals Living in Vicinity of Mining/Smelting Operations

Tissue or Fluid Type	Location	Description	Concentration	References
Hair	Yellowknife, NWT	workers from gold mining and smelting operation	mean: 27 µg/g	Dafoe, 1978
	Canada	5- to 9-year-olds in a gold-ming town	mean: 1.76 µg/g	CPHA, 1978
	Tacoma, Washington, U.S.	median of 0.3 miles from copper smelter median of 6.3 miles from copper smelter	mean: 15 µg/g mean: 11.6 µg/g	Polissar *et al.*, 1990
	U.S.	children in various copper smelter towns	median: 0.38 µg/g	Baker *et al.*, 1977
	not specified	boys living in vicinity of a power plant that burned local coal with high arsenic content	most highly exposed group: 0.6-10 µg/g mean 36 km from source: 0.3 µg/g	Bencko and Symon, 1977

Table 3-10 Arsenic Concentrations in Human Biological Tissues and Fluids from Individuals Living in Vicinity of Mining/Smelting Operations

Tissue or Fluid Type	Location	Description	Concentration	References
	not specified	fourth grade boys living in cities representing arsenic exposure gradients	highest exposure group mean: 9.1 µg/g lowest exposure group mean: 0.3 µg/g	Hammer *et al.*, 1971
	Northern Palatinate Region of Germany	294 residents from areas of high As ores and former mining activity	range: <0.005 to 0.682 µg/g mean: approx. 0.05 µg/g	Gebel *et al.*, 1998
	Ireland	5- to 12-year-olds living near a cast metal mine	mean: 2.1 µg/g	Corridan, 1974
	San Luis Potosi, Mexico	urban area near smelter (children) urban area 7 km from smelter (children)	range: 1.4 to 57.3 µg/g mean: 9.87 µg/g range: 0.4 to 1.8 µg/g mean: 0.84 µg/g	Díaz-Barriga *et al.*, 1993
	Japan	primary-school boys living near a smelter	geometric mean: 2.1 µg/g	Suzuki *et al.*, 1974
	Ajo, Arizona, U.S.	within 2 miles of copper mine and smelter (M and F children aged 5 to 18)	mean: 2.22 µg/g	Morse *et al.*, 1979
Urine	Silver Creek Mine, Park City, Utah, U.S.	urine samples from 127 M and F community members; range of ages; urine concentrations not corrected for creatinine or specific gravity	range: 4 to 66.5 µg/L mean: 19 µg/L	ATSDR, 1988
	U.S. communities near mining operations	concentrations in urine of children	speciated arsenic 8 to 13.3 µg/L	Binder *et al.*, 1986; Colorado Dept of Health, 1987; Butte-Silver Bow, 1992
	Tacoma Washington	children in vicinity of smelting operation	speciated arsenic 18.4 to 19.6 µg/L	Kalman *et al.*, 1990
	Tacoma, Washington, U.S.	-median of 0.3 miles from copper smelter -median of 6.3 miles from copper smelter	speciated arsenic -mean: 19.4 µg/L -mean: 11.7 µg/L	Polissar *et al.*, 1990

Table 3-10 Arsenic Concentrations in Human Biological Tissues and Fluids from Individuals Living in Vicinity of Mining/Smelting Operations

Tissue or Fluid Type	Location	Description	Concentration	References
	Murray Smelter, Salt Lake County, Utah, U.S.	37 M and F residents; range of ages	range: <2 µg/L to 3.7 µg/L	ATSDR, 1997
	Ajo, Arizona, U.S.	within 2 miles of copper mine and smelter (M and F children aged 5 to 18)	mean: 47.5 µg/L	Morse *et al.*, 1979
	ASARCO smelter, Tacoma, Washington	children aged 2 to 6 years living within 0.3 km of smelter	speciated arsenic range: 2.81 to 127 µg/L mean: 48.2 µg/L (post-shutdown, 0 to 66.9, mean 16 µg/L)	Lee and Kissel, 1995
	Anaconda, Montana	children from variety of locations near former copper smelter site	total arsenic mean: 19.1 µg/L speciated arsenic 8.6 µg/L (close 9.5, remote, 7.1 µg/L)	Hwang *et al.*, 1996
	Mill Creek, Anaconda, and Opportunity, Montana	M and F children, aged 2-6 yrs from towns adjacent to (and downwind of), upwind of, and 6 km downwind of former copper smelter site, respectively	total arsenic range of means: 10.6 to 66.1 µg/L range of means: 16.1 to 53.8 µg/g (adjusted for creatinine)	Binder *et al.*, 1987
	U.S.	Men exposed to arsenic in a smelter in 1953	average: 820 µg/L median: 580 µg/L	Pinto and McGill, 1953
	U.S.	Men exposed to arsenic in a smelter in 1976	average: 174 µg/L range: 38-539 µg/L	Pinto *et al.*, 1976
	U.S.	Children in 11 copper smelter towns	geometric mean: 19 µg/L	Baker *et al.*, 1977
	U.S.	Children in most heavily arsenic-contaminated town of 11 copper smelter towns	geometric mean: 18 µg/L	Baker *et al.*, 1977

Table 3-10 Arsenic Concentrations in Human Biological Tissues and Fluids from Individuals Living in Vicinity of Mining/Smelting Operations

Tissue or Fluid Type	Location	Description	Concentration	References
	Ruston enclave, Washington, near Tacoma smelter	Grade 3 and 4 children (M, F) living within 1 mile of smelter	total arsenic range of means: 80 to 300 µg/L	Milham and Strong, 1974
	San Luis Potosi, Mexico	urban area near smelter (children) urban area 7 km from smelter (children)	total arsenic range: 69 to 594, mean 191.1 µg/g creatinine range: 41 to 143, mean 87.5 µg/g creatinine	Díaz-Barriga *et al.*, 1993
	Northern Palatinate Region of Germany	294 residents from areas of high As ores and former mining activity	range: <0.1 to 23.8 µg/L (24h) mean: approx. 5.8 µg/L (24h)	Gebel *et al.*, 1998
	Hettstedt, Germany	M and F children, 5-14 yrs of age, from region of historically intense copper mining and smelting	total arsenic range: 0.2 to 70.6 µg/L	Trepka *et al.*, 1996
	Belgium	children living less than 1 km and 2.5 km from smelting facility	speciated arsenic 20 to 30 µg/g creatinine, 17 to 38 µg/g creatinine	Buchet *et al.*, 1980b
	Devon and Cornwall, UK	residents near areas of past intense mining and smelting of arsenical ores; male children and M and F adults	total As without arsenobetaine range: 2.7 to 58.9 µg/L	Kavanagh *et al.*, 1998
	Sweden	workers in an arsenic trioxide refinery	speciated arsenic 140 to 360 µg/g creatinine	Vahter *et al.*, 1986
	Japan	42 workers in a copper smelter	average: 56 µg/L	Kodama *et al.*, 1976
	Lavrion, Greece	children living near areas of historical lead mining and smelting activity	total arsenic range: 0.53 to 77.23 µg/24 hr	Eikmann *et al.*, 1991
	Lavrion, Greece	adults living near areas of refinery operations	total arsenic 1.7 to 193 µg/24 hours	Eikmann *et al.*, 1991
	not specified	copper smelter workers	total arsenic 52 to 66 µg/L	Smith *et al.*, 1977

Table 3-10 Arsenic Concentrations in Human Biological Tissues and Fluids from Individuals Living in Vicinity of Mining/Smelting Operations

Tissue or Fluid Type	Location	Description	Concentration	References
	not specified	Women living in village 5 km from smelter	total arsenic mean: 50 µg/L	Holmqvist, 1975
	not specified	Smelter employees	average: 540 µg/L	Lundgren, 1954
Whole blood	Endemic area of blackfoot disease, Taiwan[a]	Blackfoot disease patients and members of their family	mean: 60 µg/L	Heydorn, 1969
Red cells	Endemic area of blackfoot disease, Taiwan[a]	Blackfoot disease patients and members of their family	mean: 93 µg/L	Heydorn, 1969
Plasma	Endemic area of blackfoot disease, Taiwan[a]	Blackfoot disease patients and members of their family	mean: 30 µg/L	Astrup, 1968; Heydorn, 1969

[a] This area is not in the vicinity of a mining/smelting operation; however, the drinking water contained unusually high levels of arsenic (mean concentrations in well water ranged from 54 to 743 µg/L).

For the purposes of comparison, the following table, providing data on urinary arsenic concentrations in persons exposed to point sources of arsenic (occupational or extreme environmental arsenic levels) was included.

Table 3-11 Arsenic Concentrations in Human Urine from Individuals With Exposures to Known Sources of Arsenic Other than Mining/Smelting

Location	Description	Concentration	References
Mexico	residents of areas with high natural levels of arsenic (drinking water exposure)	total arsenic: 307 to 464 µg/L	Concha *et al.*, 1998
Chile	residents of areas with high natural levels of arsenic (drinking water exposure)	speciated arsenic: 544 µg/g creatinine	Del Razo *et al.*, 1997
Cornwall, U.K.	Occupationally exposed adults	speciated arsenic: 50 to 245 µg/L	Farmer and Johnson, 1990
Belgium	Occupationally exposed adults (arsenic trioxide)	speciated arsenic: 74 to 934 µg/L	Buchet *et al.*, 1980a

Table 3-11 Arsenic Concentrations in Human Urine from Individuals With Exposures to Known Sources of Arsenic Other than Mining/Smelting

Location	Description	Concentration	References
Finland	residents of areas with high natural levels of arsenic (drinking water exposure)	speciated arsenic: 58 µg/L	Kurttio *et al.*, 1998
Sweden	Occupationally exposed adults (arsenic metal plant)	speciated arsenic: 44 to 75 µg/L	Vahter *et al.*, 1986
unspecified	Occupationally exposed adults	speciated arsenic: 45.4 to 57.2µg/L	Yamauchi *et al.*, 1989; Yamamura and Yamauchi, 1980

4.1 Estimated Daily Intake of Inorganic Arsenic by Canadians Living Near Point Sources

The estimated daily intake of inorganic arsenic by Canadians living near point sources of arsenic contamination from all exposure pathways was estimated to range from <0.1 to 35 µg/kg body weight/day, with the greatest exposure occurring in infants and young children (CEPA, 1993). The total EDI values, in µg/kg body weight/day for all age classes assessed in CEPA (1993) were <0.1 to 14 (0 to 5 yrs); <0.4 to 35 (0.5 to 4 yrs); <0.2 to 23 (5 to 11 yrs); <0.1 to 11 (12 to 19 yrs); and <0.1 to 12 (20 to 70 yrs). Cigarette smoking would likely contribute an additional 0.01 to 0.04 µg/kg body weight/day in adolescents and adults (CEPA, 1993). It should be noted that these estimates were based on limited point source monitoring data from several geographic locations in Canada, representing an unlikely "worst case scenario". Furthermore, data used in these estimates were collected before 1991, and it was assumed that 37% of the arsenic content of foods was inorganic. These estimates would likely change if the recent daily Canadian dietary intakes of inorganic arsenic from Yost *et al.*, (1998) and environmental data specific to Ontario, were to be incorporated into the calculations used in CEPA (1993). Furthermore, it should be noted that estimates of daily arsenic intake from individuals living near mining/smelting areas, or any other significant point source of arsenic contamination will vary widely depending on the site-specific arsenic concentrations that are present, which are influenced by a variety of physical and chemical site characteristics (*e.g.*, geology, hydrology, soil chemistry, water chemistry, climate weather patterns etc.).

5.0 STRATEGIES TO MITIGATE HUMAN ARSENIC EXPOSURE AT MINE/SMELTER SITES

It is clear from the data presented in Section 4.0, that human exposure to arsenic can be substantially greater for individuals living in the vicinity of mining and smelter activities, compared to individuals that are only exposed to ambient arsenic concentrations. At a number of locations, research has been undertaken to identify means of reducing arsenic exposure for populations living in close proximity to mining and smelting operations. As ingestion is the major exposure route for both point source and ambient exposure scenarios, it is not surprising that the majority of mitigation approaches have targeted the oral exposure pathway (ingestion of foods, soils/dusts, drinking water) by attempting to reduce arsenic bioavailability and exposure from contaminated soils and waters.

In previous mine/smelter health risk assessments, recommendations for the mitigation of human arsenic exposure have included covering the contaminated soil or tailings with clean topsoil (ATSDR, 1988; 1997), removal of contaminated soils or fill (ATSDR, 1997), stabilization of tailings (ATSDR, 1996), behavioural controls (*e.g.*, avoidance of sites, wash hands frequently) (ATSDR, 1988), and even relocation of some residents (ATSDR, 1987). These types of controls have varying levels of efficacy and are not always the most practical and cost-effective solutions; thus a number of exposure mitigation alternatives have been suggested.

One suggested approach involves the use of soil liming. Liming is a well-established and effective treatment method for immobilizing trace metals. The addition of lime to soils elevates pH, resulting in lower concentrations of the highly soluble and mobile free metal cations, and higher concentrations of insoluble metal salts (Neuman *et al.*,1993). However, the use of liming to remediate arsenic-contaminated soils and mine tailings may actually mobilize arsenic, as arsenic sorption reactions with oxides and silicates are pH-dependent (Jones *et al.*, 1997). Studies with tailings from the former Anaconda, Montana copper smelter site found that following liming, soluble arsenic concentrations correlated more with pH than with total arsenic concentrations. Two low pH tailings samples were found to have soluble arsenic concentrations 10 to 400 times higher after liming treatment than was observed before treatment. Thus, it was concluded that soluble inorganic arsenic species are mobilized from tailings treated with lime, and that any application of lime to arsenic-contaminated tailings or soils should carefully evaluate potential impacts of the mobilized arsenic on nearby water bodies (Jones *et al.*, 1997).

Solidification/stabilization (S/S), also known as chemical fixation or encapsulation, is a method that is widely used to reduce exposures to cationic heavy metals in contaminated soils and waste streams (Buchler *et al.*, 1996). In general, the technology involves the use of a cement or other binding agent to solidify the waste (if necessary), and depending upon the constituents of the waste and the binder, limits contaminant mobility, which may reduce the water solubility of contaminants, with subsequent reductions in exposure and toxicity potential. Recently, S/S has been proposed as a means of mitigating waste materials contaminated with arsenic (Buchler *et al.*, 1996). However, this technology is relatively new and does not appear to have been tested at mine or smelter sites. In addition, there are

presently a number of concerns and uncertainties relating to the varying solubilities and leachability of the arsenic species that may be present in waste materials at different pH levels, and the complex environmental transformations of arsenic that can occur under field conditions. Experiments by Buchler *et al.,* (1996) have concluded that the specific arsenic species subjected to S/S has a major influence on the leachability of arsenic compounds from the matrix. Further research is needed before S/S could be considered a candidate technology for the mitigation of arsenic exposure at mine/smelter sites.

Historically, the addition of iron, aluminum, zinc, manure or organic matter to arsenic-contaminated soils has been found to reduce arsenic bioavailability to terrestrial organisms, as the soluble inorganic arsenic species become bound or complexed to compounds that have a much lower solubility (Liebig, 1966; NRCC, 1978). However, the large amounts of iron or aluminum that are often required may make this approach uneconomical (Walsh *et al.,* 1977). Phosphate addition has also been used to treat arsenic-contaminated soil but is not always effective. While phosphates generally outcompete arsenates for plant root uptake, they also compete with arsenate for fixation sites on clay particles. Thus, phosphate addition can mobilize arsenate from adsorption sites where it was previously unavailable to biota (Woolson, 1973). Nonetheless, a 10:1 phosphate to arsenate ratio has generally been found to be an effective treatment for minimizing arsenic bioavailability in soil, especially if deep plowing is conducted concurrently (Walsh and Keeney, 1975). Deep plowing on its own has also been found to be effective as it exposes the As(V) and As(III) species to a greater number of fixation sites in the soil (Walsh *et al.,* 1977). Deep plowing is typically conducted by growing tolerant cover crops on the arsenic-impacted soil, then plowing them under.

There are a number of chemical treatment methods for removing arsenic from solution that have been used in situations where drinking water supplies or mine site wastewaters have contained high arsenic concentrations. Many of these methods have been in use for decades and include sedimentation, ion exchange, coprecipitation, addition of alum, iron compounds, sodium sulfide, calcium oxide, and sodium, aluminum or iron hydroxides (Rosehart and Lee, 1972; Gulledge and O'Connors, 1973; Shen, 1973). The arsenic removal efficiency of these methods typically ranges from 50 to 100%, depending on the duration of treatment time, the concentrations of chemical treatment used, and a number of water quality parameters (*e.g.*, pH).

No other potential technologies for the mitigation of arsenic exposure at mine/smelter sites were identified in the literature reviewed.

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CANTOX ENVIRONMENTAL

DELORO VILLAGE
EXPOSURE ASSESSMENT AND HEALTH RISK CHARACTERIZATION FOR ARSENIC AND OTHER METALS

PART 4 - TOXICOLOGICAL REVIEW FOR ARSENIC AND OTHER METALS

December, 1999

PART 4
TOXICOLOGICAL REVIEW OF ARSENIC AND OTHER METALS

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PART 4.1
TOXICOLOGICAL REVIEW OF ARSENIC AND OTHER METALS

4.1.0 INTRODUCTION

This Part contains critical literature on the health effects, exposure limits and bioavailability of chemicals of concern for the current assessment. The general purpose of this Part is not to provide a complex dissertation discussing every published study on every chemical. Rather, it is meant to provide a review of crucial studies only, for the purpose of establishing an exposure limit or a concentration of each chemical of concern that a person could be exposed to on a daily basis without expecting to incur adverse health effects. In the case of arsenic, given the level of concern regarding exposure to this chemical, a comprehensive review of pharmacokinetics, toxicology and carcinogenicity was conducted, and is presented here.

The methodology used in the derivation of exposure limits, as well as the importance of consideration of bioavailability in hazard assessment, are detailed in Part 2, Section 3.0. In general, for the current assessment, regulatory-based exposure limits were identified from the scientific literature, where available. A literature review was undertaken in order to provide information on the toxicological database for each of the chemicals of concern. The studies that form the bases of the exposure limits were discussed in conjunction with other important studies and critical literature that has been published since the derivation of the exposure limit. The types of studies presented within the hazard assessment include both long- and short-term studies on animals and humans, where data were available. A lack of inclusion of certain types of studies (*e.g.*, reproductive, multi-generational, human studies) indicates that either these types of studies were not identified for the particular chemical of concern in the literature reviewed or that the data located were considered irrelevant.

In some cases there were no specific data regarding the bioavailability of a chemical following respiratory exposure. In these instances, the bioavailability following inhalation was estimated, based on airborne particle dynamics in the human respiratory system and on the environmental behaviours of chemicals in relation to tendency to be present in a vapour state versus adsorbed to particulate matter. A detailed discussion of these issues, and how they were applied to the current risk assessment, is provided in Appendix A.

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PHARMACOKINETICS AND TOXICOLOGY: ARSENIC

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PART 4.2
ARSENIC: PHARMACOKINETICS AND TOXICOLOGY

4.2.1 PHARMACOKINETICS

Pharmacokinetics describe the behaviour of a chemical within the body, including absorption or uptake into the body *via* different routes of exposure, metabolism and distribution of the chemical or its metabolites within the tissues of the body, as well as rates and mechanisms of excretion or elimination from the body.

Several arsenical compounds are discussed in the following sections, including inorganic forms: trivalent arsenic (As[III]), the valency found in arsenite (AsO_3^{3-} or AsO_2^{1-}) and arsenic trioxide; pentavalent arsenic (As[V]), the form found in arsenate (AsO_4^{3-}, $HAsO_4^{2-}$, or $H_2AsO_4^{1-}$); as well as organic arsenic compounds: monomethylarsonic acid (MMA; $CH_3AsO[OH]_2$) and dimethylarsinic acid (DMA; $[CH_3]_2AsO[OH]$), the predominant metabolites of inorganic arsenic in humans; as well as arsenobetaine ($[CH_3]_3As^+CH_2COOH$) and arsenocholine, organic arsenicals found predominantly only in fish and seafood. For the purposes of this discussion, the term seafood is meant to indicate fish shellfish (crustaceans and bivalves) derived from marine environments for human consumption, and does not include seaweed- or kelp-based products.

4.2.1.1 Absorption

4.2.1.1.1 Absorption Following Oral Exposure

Factors influencing the absorption of arsenic from the gastrointestinal tract include:

- the specific speciation of the arsenic compound under consideration;
- the physical-chemical properties of the arsenic, especially its solubility;
- the magnitude of the dose;
- the matrix in which the exposure is received; and,
- the animal species, especially the physiological characteristics of the digestive system (U.S. EPA, 1984a, 1984b).

With regard to matrix effects, it is generally true that the greater the solubility of arsenic in the matrix in which it is present, the better the absorption (NAS, 1977).

The impacts of the factors described above on the oral bioavailability of arsenic compounds, as outlined in the published literature, are discussed below.

Greater than 95% of water-soluble inorganic trivalent arsenic may be absorbed from the gastrointestinal tract of humans (Coulson *et al.*, 1935; Ray-Bettley and O'Shea, 1975; Pomroy *et al.*, 1980). Similarly, the results of animal studies indicate that soluble arsenic

compounds are readily absorbed following oral exposure, based on proportions of the administered dose of arsenic recovered in the faeces. For example, the percentage absorption ranges between 68 to 98% (mice and monkeys), 60 to 90% (hamsters) and 51 to 67% (rabbits and rats) (Charbonneau *et al.*, 1978a,b; Vahter and Norin, 1980; Odanaka *et al.*, 1980; Yamauchi and Yamamura, 1985; Marafante *et al.*, 1987; Marafante and Vahter, 1987; Freeman *et al.*, 1993; 1995). Reduced oral bioavailability is observed with the less soluble forms of arsenic (arsenic trisulfide, lead arsenate, arsenic triselenide) in both humans (Mappes, 1977) and laboratory animals (Marafante and Vahter, 1987).

The oral bioavailability of inorganic arsenic has been reported to be considerably reduced when administered in a soil or dust matrix. The oral bioavailability of arsenic associated with a soil matrix was 24% in rabbits, when normalized for concentrations of arsenic in urine following intravenous (i.v.) administration of the same compound (Freeman *et al.*, 1993). Freeman *et al.* (1995) studied the bioavailability of arsenic in soil and house dust from the vicinity of a mine and smelter facility following administration to female Cynomolgus monkeys *via* gel capsules. The mean absolute percentage oral bioavailability values were reported to be 19 and 14% (based on normalization for urinary concentrations following i.v. administration) or 10 and 11% (based on normalization for blood concentrations following i.v. administration) for arsenic in house dust and soil matrices, respectively. These values are in agreement with that of Groen *et al.* (1994), who reported the oral bioavailability of inorganic arsenic in a bog ore-containing soil matrix was 8.3% in dogs, based on normalization of urinary excretion following i.v. administration. The basis for the reduction of bioavailability of arsenic compounds in soils and house dusts in the vicinity of mining and smelter operations is related to the fact that arsenic from these sources tend to be in less soluble forms (*e.g.*, metal-arsenic oxides and phosphates) and, as a result of containment within a solid matrix, to be less accessible for dissolution or uptake (Davis *et al.*, 1996).

There were no data in the published literature for the bioavailability of inorganic arsenic compounds in food. The OMOE (MOEE, 1994) cited an assumed value of 90% absorption of arsenic compounds in various food types; however, this value appears high given the information presented above on studies of various inorganic arsenic species.

Organic arsenic compounds, including arsenocholine, MMA and DMA, are readily absorbed following oral administration in humans and laboratory animals, with absorption reported to be greater than 75% (Stevens *et al.*, 1977; Buchet *et al.*, 1981a; Yamauchi and Yamamura, 1984; Marafante *et al.*, 1987; Yamauchi *et al.*, 1988).

In summary, the oral bioavailability of arsenic compounds is greatly dependent both on chemical species and on the matrix in which it is administered. Based on the published literature, the absorption of water-soluble inorganic arsenic compounds in an aqueous solution is about 95%, that of soil- and house dust-bound arsenic is about 14 and 19%, respectively.

4.2.1.1.2 Absorption Following Inhalation Exposure

The fraction of arsenic absorbed from the lung is dependent on particle size, as it affects transportation of particles into the lower regions of the lung, and the chemical species of arsenic. The published literature indicates that the key parameters upon which pulmonary absorption of arsenic depends includes particle size and resultant degree of deposition of particulate-borne arsenic in the lungs as well as the specific arsenic compound and its solubility. The role of airborne particle dynamics on bioavailability is discussed in greater detail in the Introduction to this Part.

The role of solubility of the chemical species on absorption in the lungs has been the subject of many studies through administration *via* intratracheal instillation. It has been reported that 95 to 99% of doses of soluble arsenic compounds (sodium arsenite, sodium arsenate, arsenic trioxide) were absorbed from the lung within 1 day (and 99.6 to 99.8% are absorbed within 3 days) following intratracheal instillation in rats and hamsters (Inamasu *et al.*, 1982; Pershagen *et al.*, 1982; Rhoads and Sanders, 1985; Marafante and Vahter, 1987); while insoluble arsenic compound (arsenic trisulfide, lead arsenate and calcium arsenate) were absorbed from the lung more slowly (98.7%, 55% and 50%, respectively, after 3 days) (Marafante and Vahter, 1987). About 64 to 74% of particulate-bound arsenic (bound to fly ash and copper smelter dust) was absorbed from the lungs of hamsters 48 hours after intratracheal administration, whereas arsenate and arsenite were completely absorbed from the lungs in the same time period, when administered with an inert dust material (Buchet *et al.*, 1995). Buchet *et al.* (1997) concluded that absorption of arsenic in the lungs depends on a combination of the following factors: chemical species, particle size, and dust load in the lung.

As mentioned earlier, absorption of particulate-bound arsenic following inhalation is greatly dependent on the dynamics of deposition, retention and clearance of airborne particles by the respiratory system. Based on the airborne particle dynamics model, the smaller airborne particles (<2 μm) are respirable and would enter and be retained in the respiratory system, and arsenic associated with these particles would be subject to absorption within the lungs. Larger airborne particles would be cleared from the respiratory system by mucociliary action and swallowed; arsenic adsorbed to these particles would be subject to gastrointestinal absorption (U.S. EPA, 1984b). Pinto *et al.* (1976) and Smith *et al.* (1977) studied the relationship between concentrations of arsenic in the urine of copper smelter workers and in workplace air, based on particle size distributions. It was noted that there was a stronger correlation between urinary concentrations and concentrations in the particulate fraction composed of larger particles (> 5 μm), indicating that in exposures to particulate-borne arsenic, clearance and swallowing of particulates, with subsequent absorption in the gut, may be a more important route of exposure.

Holland *et al.* (1959) studied the deposition and absorption of arsenic in the respiratory system of

hospitalized lung cancer patients. Arsenic-74 and arsenite aerosols were administered *via* cigarette usage. Approximately 40% of the arsenic inhaled was actually deposited in the lungs, and of this 75 to 85% was absorbed, resulting in an overall absorption of 30 to 34% (*i.e.*, 75 to 85% of 40% equals 30 to 34%). While the health status of the subjects were not controlled in this study, these results obtained are in general agreement with the range of values for arsenic absorption from the lung as discussed above, and what is known about general airborne particle dynamics. Given that, for typical exposures, about 13% of airborne particles are respirable (Brain and Mosier, 1980), and that soluble arsenic compounds are almost completely absorbed in the lungs (about 99%), of the absorption of particle-borne soluble arsenic would approximate 13%, a value lower than the range indicated by Holland *et al.* (1959). The U.S. EPA (1984a) used the lower value of 30% from Holland *et al.* (1959) to represent the fraction of inhaled arsenic that is absorbed by humans.

There were little data regarding the absorption of organic arsenic *via* inhalation; Stevens *et al.* (1977) reported that 92% of a dose of DMA was absorbed following intratracheal instillation in the rat, indicating that, like inorganic forms of arsenic, once in the lower regions of the lung, absorption of organic arsenic is almost complete.

In summary, the bioavailability of inorganic arsenic to which subjects are exposed via inhalation appears to be primarily determined by the inhalation behaviour of particulate matter, and would be in the range of 30 to 34%.

4.2.1.1.3 Absorption Following Dermal Exposure

There are few data on the absorption of arsenic compounds through the skin. Dutkiewicz (1977) conducted a study of the absorption of sodium arsenate through the skin of rats whose tails were immersed in an aqueous solution for 1 hour. Based on the observation that arsenic concentrations in blood, liver, and spleen increased over 5 days following exposure, ATSDR (1993) suggested that arsenic may initially bind to the skin and then be slowly absorbed into the blood stream even if exposure is discontinued.

Wester *et al.* (1993) quantified the *in vitro* and *in vivo* absorption of inorganic arsenic in soil and water through human and monkey skin. Dermal absorption of arsenic in monkeys from soil was reported to range from 3.2 to 4.5%, while absorption from water ranged from 2.0 to 6.4%. The reported absorption through human skin was somewhat less than through monkey skin, ranging from 0.8 and 1.9% from soil and water, respectively.

In summary, the dermal absorption of inorganic arsenic in humans has been observed to range from 0.8 to 1.9%.

4.2.1.2 Distribution

Distribution of arsenic within the body following absorption is affected by the route through which exposure occurs. The available studies indicate that oral exposure resulted in higher

initial distribution to the liver, in comparison to intravenous and subcutaneous exposures (Charbonneau *et al.*, 1979; Vahter, 1981; Marafante *et al.*, 1985). In contrast, the distribution of arsenic in the body following inhalation and intravenous exposure resulted initially in accumulation in the liver, lungs, muscle and gastrointestinal epithelium in mice, marmoset monkeys and rabbits (Lindgren *et al.*, 1982; Vahter *et al.*, 1982; Vahter and Marafante, 1983). However, given sufficient time for equilibration within the body, arsenic generally tends to be evenly distributed amongst various tissues within the body, with slight elevations in the concentrations of arsenic in nails and hair; this has been observed in humans following oral exposure (Liebscher and Smith, 1968; Kurttio *et al.*, 1998) and in mice, monkeys, rabbits and hamsters following oral, intravenous and intratracheal administration (Stevens *et al.*, 1977; Vahter and Norin, 1980; Lindgren *et al.*, 1982; Vahter *et al.*, 1982; Vahter and Marafante, 1983, 1988; Rhoads and Sanders, 1985; Yamauchi and Yamamura, 1985; Hood *et al.* 1987, 1988; Marafante and Vahter, 1987). Tissue distribution studies have demonstrated placental transfer of arsenic in mice(Hood *et al.* 1987, 1988; Lindgren *et al.*, 1984), and that arsenic can penetrate the blood-brain barrier (Ghafgazi *et al.*, 1980; Valkonen *et al.*, 1983).

Distribution of specific arsenic compounds within the body is dependent on interactions with certain tissue types (and functional groups therein), as well as physiological characteristics of different animal species. Vahter and Marafante (1983) observed that more arsenic is retained in the tissues of mice and rabbits when injected as arsenite than when injected as arsenate. This difference in distribution was believed to be due to the stronger affinity of trivalent arsenic (As[III]) for sulfhydryl groups based on the observed concentrations in sulfhydryl-rich tissues such as keratin, found in hair and nails. Indeed, regardless of the form of arsenic administered, trivalent arsenic tends to be the primary form interacting and binding to tissues in most species (Vahter and Marafante, 1983; Vahter, 1994).

Pentavalent arsenic (As[V]) may also interact with tissues; based on its similarity in chemical properties to phosphate, it may substitute for phosphate in enzyme-catalyzed reactions and become incorporated into bone (Mitchell *et al.*, 1971; Vahter, 1981; Vahter and Marafante, 1988). The metabolic fate of As(V), discussed below, tends to limit this form of tissue interaction. Arsenate also tends to be rapidly cleared from the blood stream into the kidney, where it may be excreted or, based on its similarity to phosphate, be actively reabsorbed (Vahter and Marafante, 1988). These differences in distribution between trivalent and pentavalent arsenic, dependent on mechanisms of metabolism and excretion, result in different profiles of tissue interaction and retention, and thus possibly toxic potency, as is discussed below.

There are limited data regarding the distribution of organic forms of arsenic following absorption, however, the few laboratory studies available indicate that DMA and MMA are distributed amongst all tissues of the body following oral and intratracheal exposure (Stevens *et al.*, 1977; Yamauchi and Yamamura, 1985; Yamauchi *et al.* 1988).

While the distribution of arsenic species within the body is generally similar for most species studied, including humans, a significant deviation from the distribution profile described

above is seen in the rat. In the rat, a large proportion of arsenic has been observed to bind to hemoglobin in the erythrocytes, in the form of DMA (*i.e.*, following metabolism, discussed below) (Vahter, 1994).

4.2.1.3 Metabolism

As stated above, the interaction of arsenic with various tissues is dependent on the chemical form of the arsenic. Thus, the metabolic fate of arsenic, whether administered in a trivalent or pentavalent form, as an inorganic or organic compound, are important factors in determining the internal concentrations and retention of trivalent arsenic.

The basic metabolic reactions affecting the fate of inorganic arsenic include reduction-oxidation reactions and methylation (Vahter and Marafante, 1988). Following absorption of inorganic arsenic into the bloodstream, and subsequent to the distribution and excretion, a proportion of As(V) is reduced to As(III). Vahter and Marafante (1985) observed that in the marmoset monkey, which does not possess the enzyme systems necessary for methylation, urinary excretion patterns indicated that about 80% of As(V) is readily reduced to As(III) in the blood stream. The urinary profile of arsenic compounds in other species, including humans, also indicates this rapid reduction of As(V) to As(III) (Yamauchi and Yamamura, 1979; Lerman and Clarkson, 1983; Vahter and Marafante, 1988).

Following absorption or production in the bloodstream, As(III) then undergoes oxidative methylation to form MMA and DMA. This methylation pathway has been observed in rats, mice, rabbits, hamsters, dogs, cattle and humans (Lakso and Peoples, 1975; Crecelius, 1977; Buchet and Lauwerys, 1987, 1994; Vahter and Marafante, 1988).

Based on urinary excretion patterns, the predominant metabolite of inorganic arsenic is DMA in humans, rats, mice, rabbits, hamsters and dogs (Charbonneau *et al.* 1979; Yamauchi and Yamamura, 1979; Buchet *et al.*, 1981a,b; Maiorino and Aposhian, 1985; Farmer and Johnson, 1990; Offergelt *et al.*, 1992; Hopenhayn-Rich *et al.*, 1993; 1996a,b; Yoshida *et al.*, 1997; 1998). The available data indicate that while MMA is formed in these species, only in humans is MMA a metabolite of any significance (Tam *et al.*, 1979a; Buchet *et al.*, 1981a,b; Vahter, 1981; Vahter and Marafante, 1983; 1988; Marafante and Vahter, 1987).

The literature indicates that MMA and DMA are the only metabolites of significance in humans following exposure inorganic arsenic. Very few studies have indicated the possibility of other methylated arsenic compounds being metabolites in the mammalian system. Apostoli *et al.* (1997) reported that arsenobetaine was observed in the urine of humans to whom inorganic arsenic (as arsine, AsH_3) had been administered. No external source of the arsenobetaine could be identified, and the authors concluded that its detection may have been an analytical artifact. Yoshida *et al.* (1997; 1998) reported that following exposure of rats to MMA and DMA, relatively small amounts of trimethylarsine oxide and tetramethylarsonium were detected in the urine. In general, however, the organic forms of arsenic (DMA, MMA, arsenocholine) tend to be excreted with minimal or no metabolic

changes (Buchet *et al.*, 1981a; Marafante *et al.*, 1984). In neither of these studies was inorganic arsenic of either valency formed during metabolism.

The primary site of methylation is believed to be the liver, although some methylating ability has been observed in tissues from the kidney as well (Lerman and Clarkson, 1983; Buchet and Lauwerys, 1987; Vahter and Marafante, 1988). Studies of tissue methylation of arsenic did not indicate significant methylating capacity in red blood cells, lung, brain, intestine, or kidney tissues of the rat (Buchet and Lauwerys, 1985), or in alveolar cells of rabbits (Marafante *et al.*, 1987). *In vitro* studies indicate that while arsenite is readily methylated in the cells of the liver, methylation of arsenate in the hepatocytes is minimal; in contrast, in kidney cells, much more DMA was produced following exposure to arsenate, as opposed to arsenite (Lerman and Clarkson, 1983; Lerman *et al.*, 1985). *In vivo* studies do indicate, however, that regardless of whether arsenate or arsenite was administered, the first and most predominant site of DMA formation is the liver (Marafante *et al.*, 1985). This would indicate that for *in vivo* metabolism, the fate of arsenate is reduction to arsenite with subsequent methylation, as opposed to direct methylation (Vahter and Marafante, 1988).

The importance of methylation in the liver is also indicated by the observation that, just as distribution of inorganic arsenic to the liver is greater following oral administration compared to other routes, so is the formation of DMA is also much greater in the liver (Charbonneau *et al.*, 1979; Vahter, 1981). Vahter and Marafante (1988) proposed that while the liver is the primary site of methylation for both arsenate and arsenite, the tissues of the kidney could be responsible for the methylation of that proportion of arsenate which is reabsorbed in the tubules of the kidney.

The methylation process of As(III) is mediated by enzymes known as methyltransferases, with glutathione and s-adenosylmethionine acting as cofactors in the reaction (Buchet and Lauwerys, 1985; 1987; 1988; 1994). The enzyme is believed to be a thiol-methyltransferase, through which a dithiol-arsenic intermediate functions as a methyl receptor (Thompson, 1993; Mushak and Crocetti, 1995). Laboratory studies have indicated that species lacking the methyltransferase enzyme, such as marmoset monkeys and other New World animals, do not metabolize inorganic arsenic into DMA, but rather accumulate it or excrete it as inorganic arsenic (Vahter, 1994; Aposhian, 1997). Based on the results of inhibition and substrate-substitution studies, Buchet and Lauwerys (1985; 1994) postulated that while different enzyme systems were responsible for the production of MMA and DMA in humans, the same methyl donors were used in both processes. The time-course of appearance of DMA, MMA and inorganic arsenic in the urine of humans also led several other authors (Foà *et al.*, 1984; Apostoli *et al.*, 1997) to the conclusion that there are 2 successive methylating processes responsible for production of MMA and DMA. Under normal conditions, availability of s-adenosylmethionine, which acts as the methyl group donor, is not the rate-limiting factor in the methylation of arsenic (Buchet *et al.*, 1981a; Buchet and Lauwerys, 1987). While the exact role of glutathione in the methylation reaction is not known, decreased concentrations of glutathione in the liver has been associated with decreased rates of arsenic methylation (Buchet and Lauwerys, 1987). Specifically, decreased concentrations of glutathione has been

reported to inhibit the production of DMA (Hirata *et al.*, 1989). Glutathione may play a role in the metabolic fate of arsenic at other stages, as it has been observed that availability of glutathione is also important for reduction of As(V) to As(III) and for the uptake of As(III) into hepatocytes (Lovell and Farmer, 1985; Buchet and Lauwerys, 1987; 1994).

While blood and tissue concentrations would be the most accurate measure of the degree of methylation of arsenic in the body, the proportions of inorganic arsenic and methylated metabolites in the urine also provides a measure of arsenic methylation. As discussed in Section 4.2.1.4, urinary excretion is the main pathway of elimination of arsenic, although the urinary profile does not provide information on the fraction of arsenic (generally as As[III]) retained in the body. For the reasons discussed above, the route of exposure, chemical species administered, and time following exposure can all affect the proportions of inorganic arsenic forms and their methylated metabolites. Following exposure to inorganic arsenic, the relative proportions of inorganic arsenic, MMA and DMA in the urine of humans are in the ranges of 10 to 30%, 10 to 25% and 40 to 80%, respectively (Crecelius, 1977; Smith *et al.*, 1977; Tam *et al.*, 1979b; Buchet *et al.*, 1981a,b; Vahter, 1986; Farmer and Johnson, 1990; Johnson and Farmer, 1991; Hopenhayn-Rich *et al.*, 1993, 1996a,b; Yoshida *et al.* 1998). Based on concentration profiles in the urine, arsenic has a similar metabolic fate in the hamster, mouse, rabbit and humans (Maiorino and Aposhian, 1985; Vahter and Marafante, 1988; Carmignani *et al.*, 1985; Yoshida *et al.*, 1998), although as stated earlier, MMA is a significant component only in humans. Of the species studied, the mouse has the greatest capacity for methylation, followed by rats, rabbits, humans, hamsters (Vahter and Marafante, 1988). The impact of exposure to different chemical species was investigated by Vahter and Marafante (1983), who compared the metabolism of arsenate and arsenite in mice and rabbits. It was observed that methylation of arsenite (As[III]) was much more complete than was that of arsenate (As[V]), based on the proportions of methylated and unmethylated species in the urine.

4.2.1.3.1 Differences in Individual Methylation Capacity

4.2.1.3.1.1 Individual Differences Independent of Exposure Levels

In general, humans have a lesser methylation capacity than do laboratory animals (Chan and Huff, 1997). Individual variation in methylating capacity within human populations has been associated with smoking, gender, years of exposure, and ethnic background (Hopenhayn-Rich *et al.*, 1996b). Concha *et al.* (1998b) observed that methylation efficiency was greater in pregnant women than in nonpregnant women. A significant variation in methylation capacity in a South American population led Concha *et al.* (1998a) to propose that there may be a polymorphism for methyltransferases. The population under study was chronically exposed to high levels of arsenic in the drinking water; Concha *et al.* (1998a) reported that the urine of children from this population had much higher proportions of inorganic arsenic in the urine (50%) than did adult women (32%) or children from other populations experiencing much lower exposures (18%). Genetic polymorphism for methyltransferases was also proposed by Mushak and Crocetti (1995). Although Kurttio *et al.* (1998) reported a greater capacity for

methylation in older persons, Kalman *et al.* (1990) did not observe that the methylating capacity of children differed significantly from that of adults.

4.2.1.3.1.2 Threshold of Methylation Theory

It has been theorized that arsenic exposures slightly in excess of 1 mg As/day represents a saturation threshold for the rate of methylation of arsenic in the body (Buchet *et al.*, 1981b; Marcus and Rispin, 1988; Petito and Beck, 1990; Stohrer, 1991). Based on the assumption that there was a saturation threshold for the methylation of arsenic, Valberg *et al.* (1994) calculated a saturation half-point of 0.7 µg As/day, using the Michaelis–Menton equation. The existence of such a threshold would mean that above certain exposure levels, the rate of methylation, and therefore the proportion of arsenic which is methylated would decrease, relative to the total arsenic exposure. The threshold of methylation theory is based on a limited number of human studies in which it was observed that the proportion of methylated arsenic compounds in the urine decreases in proportion to the total arsenic exposure.

Based on a comprehensive review of the literature comparing the proportions of methylated metabolites in the urine to the rates of exposure to arsenic, Hopenhayn-Rich *et al.* (1993) concluded there was no threshold for arsenic methylation capacity. Comparing proportions of methylated metabolites in the urine to doses of inorganic arsenic, no significant increase in the proportions of inorganic arsenic, or decrease in the amount of MMA or DMA was observed in humans exposed to arsenic through the workplace, drinking water or background environmental concentrations. There was a wide range of exposures, as indicated by total urinary speciated arsenic concentrations ranged from 4.4 to 245 µg As/L. Hopenhayn-Rich *et al.* (1993) did note that there appears to be a high degree of individual variability in methylation capacity.

The proponents of the methylation saturation theory suggest that the threshold is better indicated by increases in the ratio of MMA to DMA concentrations (Beck *et al.*, 1995; Slayton *et al.*, 1996). A decreased capacity for dimethylation, as indicated by decreased proportions of DMA, with chronic exposures to high concentrations of arsenic in drinking water, as compared to lower concentrations, has been reported in several human populations (Yamauchi *et al.*, 1989; Hsueh *et al.*, 1995; Del Razo *et al.*, 1997).

The opponents of the methylation saturation theory disagree that the epidemiological data indicate a significant increase in the MMA:DMA ratio (Smith *et al.*, 1995; Mushak and Crocetti, 1996). Hopenhayn-Rich *et al.* (1996a) conducted a study of the metabolism of arsenic in a Chilean population, and observed a slight increase in the proportion of inorganic arsenic, as well as a slight decrease in the MMA:DMA ratio. Subsequently, these authors studied the proportions of arsenic species in the urine following an intervention which reduced the drinking water concentrations, and observed a slight decrease in both the proportion of inorganic arsenic and the MMA:DMA ratio (Hopenhayn-Rich *et al.*, 1996b). Similarly, Warner *et al.* (1994) studied the metabolism of arsenic in a population in Nevada, comparing a group exposed to drinking water concentrations greater than 500 µg As/L versus

a group exposed to an average of 16 µg As/L, and found no significant differences in proportions of MMA and DMA in the urine. Both of these studies reported large individual variability, which statistical analysis indicated was due to ethnicity, gender, and smoking. Concha *et al.* (1998a) reported an enhanced ability to methylate with increased exposure to arsenic, as indicated by urinary concentrations or dermal symptoms of arsenic intoxication.

There have been several theories regarding the basis for a saturation of methylation in the literature. One of the theories proposes the depletion of methyl donors believed to be due to inadequate nutrition. The methylation of arsenic following absorption would be dependent on the supply of sufficient sources of methyl donors (*e.g.*, proteins and amino acids such as cysteine and methionine) (Beck *et al.*, 1995), and deficiencies in methyl donors would result in decreased capacity for methylation of arsenic. This theory is supported by several studies in the literature. Vahter and Marafante (1987) studied the impact of a methionine/cysteine reduced diet on the methylating activity of rabbits, and reported a significant decrease in methylation of inorganic arsenic following a 25% reduction in dietary intake of the amino acids. In an epidemiological study of cancer incidence in a Taiwanese village exposed *via* arsenic, Hsueh *et al.* (1995) found that malnutrition, indexed by a high consumption of dried sweet potato as a staple food, was a risk factor for skin cancer. The importance of nutrition in maintaining adequate levels of methyl donors has been proposed as a reason for increased cancer risks in subsets of the Taiwanese population, in comparison to those observed in North American populations. However, Smith *et al.* (1995) reviewed the Taiwanese intake of protein, and found it adequate by current standards. Beck *et al.* (1995), in rebuttal to the review by Smith *et al* (1995), pointed out that current standards dictate intakes required for normal bodily processes, and may not be adequate to methylate an excessive and sustained intake of arsenic.

Several authors have indicated mechanisms whereby the dimethylation phase (*i.e.*, conversion of MMA to DMA) would be inhibited. Foà *et al.* (1984) theorized, based on the time-course of MMA and DMA in the urine, that the methylation mechanisms for MMA and DMA were different, and while the rates of the mechanism for MMA was variable, that for DMA was not variable, and thus represented a rate-limiting step. In addition, the dimethylation process (conversion of MMA to DMA) has been reported to be inhibited by excess concentrations of inorganic arsenic (Buchet and Lauwerys, 1985; 1994; Vahter and Marafante, 1988; Styblo and Thomas, 1997).

4.2.1.4 Excretion

The primary pathway of elimination of inorganic arsenic and its metabolic products (*i.e.*, As[V], As[III], MMA and DMA for humans) from the body is excretion *via* the urine. Investigations of the magnitude of urinary excretion following exposure to inorganic arsenic indicate that, for oral, inhalation, and dermal administration, 45 to 85%, 30 to 65%, and 50% of the administered dose is excreted in the urine within 1 to 3 days (Holland *et al.*, 1959; Pinto *et al.*, 1976; Crecelius, 1977; Mappes, 1977; Tam *et al.* 1979a,b; Pomroy *et al.*, 1980; Buchet *et al.* 1981a,b; Vahter *et al.*, 1986; U.S. EPA, 1988; Buchet *et al.*, 1995; Apostoli *et*

al., 1997; Kurttio *et al.*, 1998). In repeat-dose studies, it has been determined that when equilibrium between intake and output was reached, urinary excretion of arsenic following oral administration to human volunteers accounted for 40 to 60% of the daily dose (Farmer and Johnson, 1990; Johnson and Farmer, 1991). Studies in mice, hamsters and rabbits indicate that urinary excretion accounts for 50 to 87% of the doses administered by intravenous injection (Odanaka *et al.*, 1980; Vahter and Marafante, 1983; Maiorino and Aposhian, 1985). About 15 to 48% of arsenic administered intratracheally to hamsters as fly ash or copper smelter dust was eliminated in the urine within 48 hours (Buchet *et al.*, 1995). Experimental results in laboratory animals for excretion *via* the urine following other routes of exposure generally support those observed for humans (Charbonneau *et al.*, 1979; Odanaka *et al.*, 1980; Vahter and Norin, 1980; Rhoads and Sanders, 1985; Marafante and Vahter, 1987), although there is interspecies variation in overall retention times, as discussed below (Vahter and Marafante, 1988).

Faecal elimination is indicative of biliary excretion and, in the case of oral administration, of the proportion of arsenic not absorbed during passage through the gastrointestinal tract. The literature indicates that this is not a significant route of elimination of arsenic for most species (Ray-Bettley and O'Shea, 1975). Following oral administration of radiolabelled arsenic acid to humans, Pomroy *et al.* (1980) observed a total faecal elimination of about 6% over 7 days. Fecal elimination in laboratory animals ranged from 33 to 49% of an orally administered dose, although following intravenous administration, only 0.8 to 1.4% was found in the faeces (Odanaka *et al.*, 1980). Dutkiewicz (1977) observed that in the rat, excretion of arsenic following dermal administration was equivalent *via* urine and feces. Vahter (1994) postulated that faeces elimination may be more important in the rat due to a greater biliary excretion which would result from glutathione being the primary thiol in rat bile.

The time course of elimination of arsenic is of relatively short duration in both humans and experimental animals. The whole body clearance of arsenic in humans following ingestion was reported to have half-times of 40 to 60 hours (Mappes, 1977; Buchet *et al.*, 1981b), while Crecelius (1977) estimated biological half-lives of inorganic arsenic and its methylated metabolites to be 10 and 30 hours, respectively. Pomroy *et al.* (1980) observed a triphasic elimination of arsenic in humans following oral administration; about 66% of the dose had a half-life of 2.1 days, 30% had a half-life of 9.5 days, and 4% had a half-life of 38 days. Data from laboratory animals generally indicate that retention of arsenic is greatly dependent on methylating capabilities as well as species-specific tissue interactions. Thus, high-methylating species such as dogs, rabbits and mice have shorter retention times, while the marmoset monkey has a longer retention time than humans (Vahter, 1981; Vahter *et al.*, 1982; Vahter and Marafante, 1983; 1988; Vahter, 1994). The rat is an exception to this trend, as it readily methylates inorganic arsenic, but due to the interaction of DMA with hemoglobin in the red blood cells of this species, overall retention times for the rat are much longer in comparison to that in humans (Vahter, 1981; Vahter and Marafante, 1988).

Studies of inhalation exposure in humans have indicated similar results to those cited above. Occupational studies indicate that urinary arsenic levels closely mirror the time-course of daily exposures (Vahter e*t al.,* 1986). Apostoli *et al.* (1997) observed a triphasic elimination profile following inhalation exposure of humans; approximately 75% of the dose was cleared with a half-life of 4 days, while the remainder had a half-life of 10 days. Studies of arsenate and arsenite retention in rats and hamsters following intratracheal instillation indicate half-lives of 1 day or less (Rhoads and Sanders, 1985; Marafante and Vahter, 1987; Buchet *et al.*, 1995), although dependent on chemical species, small amounts of arsenic may be retained in the lung with a half-time of several months (Rhoads and Sanders, 1985).

The retention of arsenic in the body is affected by the chemical species to which it is exposed. Vahter and Marafante (1983) compared the fate of arsenate and arsenite in mice and rabbits. It was observed that in the rabbit, the retention time was greater following exposure to As(III) than after exposure to As(V), based on urinary excretion profiles. Despite the greater methylation of As(III), the retention of this form through tissue interaction resulted in a longer overall retention in the body. The tissue interaction of As(III) may be partially compensated by methylation, in species with greater capacity, such as the mouse, in which there was no significant difference in the whole body retention of As(V) and As(III). Apostoli *et al.* (1997) also observed differences in retention of arsenic species. The half-lives of different chemical species ranged from 27 to 86 hours following inhalation, with the shortest half-life exhibited by As(V), followed, in order of increasing half-life, by MMA, As(III), DMA, and AsB (Apostoli *et al.*, 1997).

4.2.1.5 Urinary Excretion as a Bioindicator of Daily Exposure to Inorganic Arsenic

4.2.1.5.1 Relationship Between Arsenic Exposure and Urinary Excretion

In previous sections, the biological fate of inorganic arsenic has been discussed with regard to absorption, distribution, metabolism and excretion. Because of the importance of urinary excretion as the primary route of elimination of arsenic, concentrations of arsenic compounds in the urine is considered to be a reliable index of recent exposure to arsenic (Hindmarsh and McCurdy, 1986; Johnson and Farmer, 1989; Buchet *et al.*, 1996a; Gebel *et al.*, 1998). The objective of developing and validating a model relating urinary concentrations to daily exposures to arsenic would be to provide a non-intrusive technique for evaluating not only arsenic exposure, but to also provide an indicator of the health status of populations exposed to arsenic.

Total urinary arsenic concentrations reflect intakes of all forms of arsenic, including inorganic arsenic as well as organic arsenicals such as MMA, DMA, arsenobetaine, arsenocholine and arsenic-containing riboses (Kalman *et al.*, 1990; Goessler *et al.*, 1997). Exposure to organoarsenicals has been associated with intake of arsenic from dietary sources. Particularly high concentrations of organic arsenics have been found in seafood products (Buchet *et al.*, 1996b; Goessler *et al.*, 1997; Walker and Griffin, 1998). Organoarsenicals can

constitute the majority of the total urinary arsenic measurements in people who have recently consumed seafood (Kalman *et al.*, 1990, Goessler *et al.*, 1997). These organoarsenicals (such as arsenobetaine) are thought to be relatively non-toxic and are believed to leave the body metabolically unchanged (Vahter *et al.*, 1983; Johnson and Farmer, 1989; Kalman *et al.*, 1990; Le *et al.*, 1993; Gebel *et al.*, 1998). Specifically, ingestion of organoarsenicals has not been associated with increased concentrations of inorganic arsenic in the body, and would thus not result in toxicity at any stage of metabolism (Buchet *et al.*, 1981a; Luten *et al.*, 1982; Buratti *et al.*, 1984; Marafante *et al.*, 1984; Johnson and Farmer, 1991; Le *et al.*, 1993; Goessler *et al.*, 1997). Thus, the inclusion of these organoarsenicals in the urinary arsenic-exposure model is not relevant in terms of relating exposures to potential adverse health effects (Johnson and Farmer, 1991). Because tissue interaction, and thus toxic potency, has been attributed to primarily As(III) (Vahter and Marafante, 1988), the urinary concentration-exposure model would preferably be limited to quantifying exposures to arsenic species which are of toxicological concern (*i.e.*, As[III] or As[V]).

As discussed in previous sections, the predominant forms of inorganic arsenic and its metabolites in the human body are inorganic arsenic (*i.e.*, As[III], As[V]), MMA and DMA (Crecelius, 1977; Buchet *et al.*, 1981a,b; Vahter and Marafante, 1988; Offergelt *et al.*, 1992). Therefore, in order to capture only those arsenicals in urine which were ultimately derived from exposure to inorganic arsenic, urine analysis should be provided information on "speciated arsenic", consisting of inorganic arsenic, MMA and DMA (Buchet *et al.*, 1981a; Kalman *et al.*, 1990; Farmer and Johnson, 1990; Offergelt *et al.*, 1992; Walker and Griffin, 1998). Background sources of inorganic arsenic such as smoking, drinking water, consumption of a typical Canadian diet (MOEE, 1994; Environment Canada, 1993) will contribute to intake of total arsenic, and possibly of total inorganic arsenic, and thus must be considered in the application of the urinary arsenic-exposure model. However, it is important to note that sources of high exposures to total arsenic, such as seafood, may have little or no impact on concentrations of inorganic arsenic in the body and thus have no relevance to potential adverse health effects.

Consumption of seafood (*i.e.*, organoarsenicals) resulted in significant increases in total urinary arsenic levels, but did not result in a significant increase in urinary concentrations of inorganic forms of arsenic (*i.e.*, As(III), As(V)) and their related methylated metabolites (*i.e.* MMA and DMA) (Buchet *et al.*, 1981a; Buratti *et al.*, 1984; Foà *et al.*, 1984; Marafante *et al.*, 1984; Le *et al.*, 1993; 1994). However, several recent studies have suggested that consumption of certain types of seafood can influence speciated arsenic concentrations. Gebel *et al.* (1998) found an association between seafood consumption and concentrations of certain methylated metabolites (DMA) of inorganic arsenic in urine. Goessler *et al.* (1997) found that urinary concentrations of As(III), As(V) and MMA in a single human volunteer were not influenced by either the consumption of codfish or exposure to gaseous trimethylarsine. However, significant increases (2.8 to 4.3 µg As per g creatinine and 4.9 to 26.5 µg As per g creatinine) in the level of DMA were observed after the first and second instance of codfish consumption, respectively. Arbouine and Wilson (1992) found that mean total urinary speciated arsenic levels (*i.e.*, the total of As[III], As[V], DMA and MMA

concentrations) increased between 1.8 and 6.9 times after the consumption of various seafood products, relative to levels measured prior to consumption. This increase was attributed to the presence of DMA in seafood. Buchet *et al.* (1996b) also observed an increase in urinary concentrations of DMA following seafood consumption and postulated that DMA may be a breakdown product of arsenobetaine formed during cooking or digestion. In another study, the consumption of seaweed and kelp was reported to cause increases in not only the urinary concentrations of arsenobetaine, but also the concentration of inorganic arsenic and DMA (Le *et al.*, 1994). In a subsequent study, Le and Ma (1998) observed an increase in speciated arsenic in the urine following the consumption of arsenosugars in bivalves. Thus, attempting to relate urinary speciated arsenic concentrations to environmental exposures associated with specific point sources may be hampered by normal consumption of fish and seafood, and the possibility of additional exposures to seafood must be considered (Goessler *et al.*, 1997; Gebel *et al.*, 1998, Le and Ma, 1998).

4.2.1.5.2 The Urinary Speciated Arsenic - Daily Exposure Model

There have been several attempts to develop a model describing the relationship between urinary arsenic concentrations and the total daily exposure. Validation of this model has been undertaken through use of actual urinary concentrations and calculated daily exposures (based on environmental media of concern [*i.e.*, soil, drinking water or indoor air] and receptor characteristics such as water consumption, *etc.*). Application of the model allows the estimation of predicted urinary concentrations, based on calculated daily exposures, which are then compared to the measured urinary concentrations of arsenic. Alternately, actual urinary concentrations may be used in the model to predict daily exposure, which is then compared to the calculated daily exposures.

Vahter *et al.* (1986) attempted to correlated urinary concentrations of speciated arsenic to occupational inhalation exposures experienced by smelter workers. The best fit empirically established linear relation determined by these authors was represented by the following equation: As_{URINE} (µg As/L) = 2.90 x As_{AIR} (µg As/m^3) + 15.5. This model does not take into account differences in environmental arsenic speciation and bioavailability

Johnson and Farmer (1989) related urinary concentrations to daily exposure to inorganic arsenic in a simple model. Based on the literature and unpublished data, these authors assumed that 40 to 60% of the daily intake of arsenic is excreted in the urine. Using typical daily creatinine outputs (1.5 and 0.75 g for adults and children, respectively), urine concentrations (as µg As per g of creatinine) were converted into estimates of daily intake which were in general agreement with modelled daily intakes based on local soil and drinking water concentrations. It should be noted that the range of proportional excretion into the urine would indicate that these authors are considering a soluble form of arsenic administered *via* oral or inhalation routes of exposure (*i.e.*, approaching complete absorption). Indeed, Farmer and Johnson (1990) note that much of the available data on the absorption of arsenic is restricted to the more soluble forms, even to administration of the arsenic in solution,

which renders bioavailability estimates less relevant for the forms of arsenic typically encountered in the environment.

Walker and Griffin (1998) published the results of the application and validation of the U.S. EPA urinary arsenic model based on urinary arsenic concentrations and calculated daily exposures of young children living near a smelting facility in Anaconda, Montana. The overall study has been published in parts, the urinary arsenic analyses and exposure assessment were conducted by Calabrese *et al.* (1993) and Hwang *et al.* (1997), while the model validation was published by Walker and Griffin (1998). In order to conduct a comparison of estimated daily exposure (mg As/day), as an absorbed dose, and urinary arsenic levels (µg As/L), Walker and Griffin (1998) used the following relationship:

$$EXC = (ABS \times CF_{abs}) / (RATE \times CF_{exc})$$

Where:

EXC	=	Urinary arsenic excreted (µg As/L)
ABS	=	Estimated absorbed intake of arsenic per day for each person (mg As/day)
CF_{abs}	=	Conversion factor (1000 µg/mg)
RATE	=	Estimated Urinary output per day (mL/day)
CF_{exc}	=	Conversion factor (0.001 L/mL)

In the course of this study, very detailed site-specific exposure assessments were conducted for the children based on air, soil, indoor dust, drinking water and food (Calabrese *et al.*, 1993; Hwang *et al.*, 1997). The resultant calculated daily exposure applied to the equation above, in order to predict urinary arsenic concentrations (using measured urinary outputs for RATE), which were then compared to actual urinary arsenic concentrations from 366 children (Hwang *et al.*, 1997). The results of this comparison indicated that the predicted and actual urinary arsenic concentrations were in reasonably good agreement, especially when based on urinary speciated arsenic concentrations.

There were several factors which were considered to affect variability in the actual or predicted urinary concentrations (Walker and Griffin, 1998). These factors included:

- accuracy of assumptions regarding the soil ingestion rate;
- the exposure scenario (*i.e.*, at home versus away from home), and the impact different scenarios would have on exposure;
- the importance of exposure to soil versus indoor dust: although a small fraction of time is spent out of doors, as much as 45% of the total daily soil/dust intake is derived from outdoor soils;
- seasonality of urinary arsenic concentrations; urinary concentrations of arsenic have been reported to be highest in late spring and summer, intermediate in fall and early spring, and lowest in winter (Hwang *et al.*, 1997);
- assumptions regarding urinary output volumes,
- dietary intake of arsenic, especially with regard to impact on total arsenic concentrations following seafood ingestion; and,

- soil and dust collection methods, in that smaller particles have a higher proportion of phases to which arsenic may bind (Davis *et al.*, 1996).

There were several limitations of the model employed in this study. The model inherently assumes that 100 percent of the estimated daily absorbed intake is completely excreted *via* the urine on a daily basis, although, as cited above, several studies have shown that, at equilibrium, 40 to 60% of the oral dose of inorganic arsenic is excreted on a daily basis (Buchet *et al.*, 1981b, Farmer and Johnson, 1990). In addition, although creatinine concentrations were determined (Hwang *et al.*, 1997), the authors did not normalize the urinary arsenic concentrations, and thus did not consider the impact of urinary density.

Based on the literature review presented above, several elements are recommended for inclusion in development and use of a model describing the relationship between urinary speciated arsenic concentrations and total daily exposure to inorganic arsenic. These are summarized below:

- Exposure estimates are usually expressed as either a daily intake rate (µg As per day) or as an uptake rate per kilogram body weight (µg As per kg body weight per day), and are based on all relevant pathways of exposure. Because exposures contributing to the total may involve different pathways (*e.g.*, oral, inhalation, dermal), total daily exposures should be expressed in terms of the proportion of arsenic absorbed into the body.

- In determination of the amount of absorbed arsenic, bioavailability of arsenic for each pathway of exposure must take into consideration differences in chemical species and the matrix in which they are found. The oral absorption of water-soluble inorganic arsenic compounds which are water-, soil-, house dust- and food-borne is about 95, 14, 19, and 90%, respectively (Pomroy *et al.*, 1980; MOEE, 1994; Freeman *et al.*, 1995). Absorption of airborne arsenic, taking into account airborne particle dynamics, is 30 to 34% (Holland *et al.* 1959), while dermal bioavailability is estimated to be 0.8 to 1.9% (Wester *et al.*, 1993).
- Excretion of inorganic arsenic and its metabolites, MMA and DMA, is estimated to account for 40 to 60% of the total absorbed dose. This is based on the studies of Holland *et al.* (1959), Buchet *et al.* (1981b) and Farmer and Johnson (1990), in which urinary excretion of soluble arsenicals (*i.e.*, for which absorption in the gut or lung would be almost complete) approximates an average of 50%.

- Urinary arsenic concentration is a surrogate for daily urinary excretion at equilibrium (*i.e.*, when, based on a relatively constant chronic daily intake, the total daily arsenic excretion is relatively constant). As such, it could be expressed as the amount of arsenic excreted in the urine per day, but this would require monitoring of urinary output over a 24 hour period. It is more convenient to take a limited number of urine samples for arsenic analysis (to determine µg As per L of urine), but these concentrations must be related back to total daily excretion, by taking into account

varying densities of the urine during the day (*e.g.*, the first void of the morning is generally more concentrated, and more dense). In order to standardize urinary concentrations, they are generally compared to concentrations of creatinine, a by-product of protein metabolism, whose daily rate of elimination is relatively constant (estimated based on typical daily urine volumes and daily creatinine excretion rates), and whose concentration in the urine would also increase or decrease based on density. Urine concentrations normalized based on creatinine are expressed as µg As per g creatinine. In the application of the urinary arsenic-exposure model, actual urine concentrations for each individual should be normalized using actual creatinine concentrations from the same individual, while the predicted urine concentrations would be normalized using the typical creatinine concentration.

- In both validation of the urinary arsenic-exposure model, and in application of the model in order to estimate daily exposures to inorganic arsenic, speciation of the arsenic in the urine is of utmost importance. In terms of potential toxicity, exposure to inorganic is the primary form of relevance, even though typical consumption patterns would result in much higher exposures to arsenic in organic forms, such as arsenobetaine. The scientific literature indicates that the biological fate of inorganic arsenic in humans is to be retained (mainly as As[III]), or to be excreted predominantly in the urine unchanged or as MMA or DMA. Therefore, in order to restrict the urinary arsenic measurement to that derived from inorganic forms, the analysis should be limited to "speciated arsenic": inorganic arsenic (As[III] and As[V]), MMA and DMA.

4.2.2 TOXICOLOGY

4.2.2.1 Systemic Toxicity

4.2.2.1.1 Animal Studies

There is some evidence which suggests that inorganic arsenic is an essential nutrient in goats, chicks, mini pigs and rats (NRC, 1989).

Acute effects of oral arsenic exposure include vomiting, nausea, diarrhea, gastrointestinal haemorrhage, and death (Levin-Scherz *et al.*, 1987; Saady *et al.*, 1989). Oral LD_{50} values (single doses that result in death of 50% of the animals) for arsenite, arsenate and arsenic trioxide in rodents have been reported to range between 10 and 110 mg As/kg bw (Dieke and Richter, 1946; Harrisson *et al.*, 1958; Gaines, 1960; IARC, 1980; Kaise *et al.*, 1989; Brown and Kitchin, 1996). Effects in acute repeat-dose studies include gastrointestinal irritation (with symptoms of vomiting and diarrhea) and mild histological changes of the liver (enlargement of bile ducts) (Heywood and Sortwell, 1979).

The lowest no-observed-adverse-effect-level (NOAEL) for short-term (13 day) oral arsenic exposure was reported to be 2.8 mg As/kg body weight/day, with a lowest-observed-adverse-effect-level (LOAEL) of 5.7 mg As/kg body weight/day, based on gastrointestinal and renal effects in monkeys fed arsenic in milk (Heywood and Sortwell, 1979).

The limited data available regarding acute dermal toxicity in the scientific literature indicate that arsenic is not likely to cause lethality or systemic toxicity. No effects were observed in guinea pigs and rats following single dermal doses of 4000 mg As/L of As(V) or 580 mg As/L of As(III) (Wahlberg and Boman, 1986), and doses up to 1000 mg As/kg bw as As(III) or As(V) (Gaines, 1960), respectively.

Studies of the oral subchronic exposures to arsenic have indicated gastrointestinal, hematological, hepatic and renal (ranging from slight abnormalities in the renal mitochondria to tubular necrosis) effects in rats, rabbits and mice (Brown *et al.*, 1976; Prukop and Savage, 1986; Jaghabir *et al.*, 1989; NTP, 1989). Cardiovascular effects in rats, including a decrease in vasoreactivity due to vascular thickening and occlusion, have also been reported to result from a sub-chronic oral arsenic exposure (Bekemeier and Hirschelmann, 1989). The lowest LOAEL from subchronic oral studies was 2.3 mg As/kg body weight/day, based on intestinal hyperemia, hepatocellular degeneration, and interstitial nephritis in rabbits (Jaghabir *et al.*, 1989), while the NOAEL for subchronic exposures would be 1.4 mg As/kg body weight/day, based on a lack of renal effects in rats (NTP, 1989). The NOAELs for mice and dogs (29.6 and 4.6 mg As/kg body weight/day, respectively) indicate that these species may be less susceptible to arsenic toxicity (Neiger and Osweiler, 1989; NTP, 1989).

Kerkvliet *et al.* (1980) observed no evidence of immunosuppression in mice administered up to 20 mg As/kg body weight/day *via* oral administration for 10 to 12 weeks. However, damage to alveolar macrophages, in the absence of direct cytotoxicity, has been reported in mice following administration of arsenic trioxide *via* inhalation (0.5 mg As/m^3 for 4 weeks), Aranyi *et al.* (1985), as well as in rats exposed to arsenite and arsenate *via* intratracheal instillation (Lantz *et al.*, 1994, 1995).

Other studies provided evidence of the immunotoxicity of arsenic (Blakely *et al.*, 1980), including decreased viral resistance (Gainer and Pry, 1972; Gainer, 1972) and decreased cell mediated immunity (Hong *et al.*, 1989; Rosenthal *et al.*, 1989). Several studies indicated possible enhancement of immunity, as indicated by delayed tumorigenesis (Schrauzer and Ishmael, 1974; Kerkvliet *et al.*, 1980). In a review of the immunotoxicity of arsenic, Burns *et al.* (1994) concluded that at high rates of exposure, arsenic exerted an immunosuppressive effect, while at lower doses, arsenic has the ability to enhance certain facets of the immune system.

Dermal exposure to 2.5 mg As/kg bw for 18 weeks, 11 times a week, was reported to result in local hyperplasia and skin irritation in mice (Boutwell, 1963).

In studies of chronic duration, mortality has been observed in dogs and monkeys administered inorganic arsenic at doses about 3 mg As/kg body weight/day, for 2 years in the diet, and for 1 year in milk, respectively (Byron *et al.*, 1967; Heywood and Sortwell, 1979). Chronic oral arsenic exposure was also reported to result in hepatic effects including enlargement of the bile duct and pathological lesions in rats (Byron *et al.*, 1967; Hisanaga, 1982) and pigmentation of liver macrophages in dogs (Byron *et al.*, 1967). Cardiovascular effects, consisting of reduction of stroke volume and cardiac output and increased vascular resistance, were observed in rats and rabbits administered As(III), although no such effects were observed at the same dose level of As(V) (Carmignani *et al.*, 1985). Other effects include depression of body weight gains and mild anaemia in dogs (Byron *et al.*, 1967).

Chronic exposure to arsenic has also been associated with persistent changes in the concentrations of neurotransmitter substances in the brains of developing and adult Wistar rats (Nagaraja and Desiraju, 1993). The NOAEL for chronic oral arsenic exposure was 1.2 mg As/kg body weight/day, while the LOAEL (based on decreased body weight gains and reduced survival) was 3.1 mg As/kg body weight/day, based on the study of effects in dogs exposed to arsenic in the diet for 2 years (Byron *et al.*, 1967). No studies were located regarding chronic effects of inhalation or dermal exposure of inorganic arsenic.

4.2.2.1.2 Human Studies

In humans, acute effects of arsenic ingestion include gastrointestinal irritation (nausea, vomiting, diarrhea and gastrointestinal bleeding), and mortality (either from fluid loss and circulatory failure or secondary to tissue damage) (Armstrong *et al.*, 1984; Fincher and Koerker, 1987; Levin-Scherz *et al.*, 1987; Campbell and Alvarez, 1989; Saady *et al.*, 1989). Minimum lethal oral doses for humans have been reported to be in the range of 1 to 3 mg As/kg (Vallee *et al.*, 1960; Armstrong *et al.*, 1984). Other effects from acute and sub-acute doses include haematological effects (anemia and leukopenia), hepatic effects (hepatitis and elevated serum transaminase levels), renal effects (proteinuria and elevated serum creatine), respiratory effects (haemorrhagic bronchitis), neurotoxicity (encephalopathy [with symptoms ranging from confusion, lethargy, headache, seizures to coma], peripheral neuropathy, acute demyelinating polyneuropathy) (Armstrong *et al.*, 1984; Fincher and Koerker, 1987; Greenberg, 1996). The acute oral LOAEL in humans was 1 mg As/kg body weight/day for these effects (Armstrong *et al.*, 1984).

Although there are many studies of the effects of arsenic inhalation in humans, there were no cases of lethality or severe impacts from short-term exposure in the scientific literature. This was interpreted by ATSDR (1993) as an indication that mortality is not likely to be of concern, even at the very high exposure levels (1 to 100 mg As/m^3) that were once associated with workplace exposures.

Subchronic exposures *via* oral administration have been reported to result in cardiovascular effects (abnormal electrocardiogram), gastrointestinal irritation, haematological effects (anaemia and leukopoenia), hepatic effects (mild hepatomegaly), and dermal effects

(conjunctivitis, edema of eyelids, and hyperkeratosis) (Holland, 1904; Mizuta *et al.*, 1956; Wagner *et al.*, 1979; Franzblau and Lilis, 1989). There was no NOAEL for sub-chronic oral arsenic exposure; while some systems were unaffected at 0.05 mg As/kg body weight/day, this value was the LOAEL, based on the effects cited above, which were observed in humans fed arsenic for 2 to 3 weeks (Mizuta *et al.*, 1956).

Health effects of subchronic and chronic occupational exposures to arsenic dusts *via* inhalation tend to be related to the irritation of mucous membranes (sequelae include generally mild laryngitis, bronchitis, or rhinitis, and, at high concentrations, perforation of the nasal septum) (Dunlap, 1921; Perry *et al.*, 1948; Pinto and McGill, 1953; Morton and Caron, 1989), and, at high concentrations, the gastrointestinal tract (resulting in nausea, vomiting, and diarrhea) (Beckett *et al.*, 1986; Bolla-Wilson and Bleecker, 1987; Morton and Caron, 1989). These effects typically lapsed upon cessation of exposure usually disappeared if exposure ceases. A NOAEL air concentration for subchronic inhalation exposure was 0.11 mg As/m^3 of inorganic arsenic for 2 months *via* inhalation, the only effects at this concentration were nausea and anorexia in 1 worker (Ide and Bullough, 1988).

Chronic exposures, usually through environmental or occupational contamination (*e.g.*, drinking water or air) have been investigated in many human populations, for oral exposures (Franklin *et al.*, 1950; Silver and Wainman, 1952; Wade and Frazer, 1953; Heyman *et al.*, 1956; Chhuttani *et al.*, 1967; Tseng *et al.*, 1968; Borgono and Greiber, 1972; Morris *et al.*, 1974; Rosenberg, 1974; Zaldivar, 1974, 1977; Hindmarsh *et al.*, 1977; Tseng, 1977; Zaldivar and Guillier, 1977; Szuler *et al.*, 1979; Mizuta *et al.*, 1956; Wagner *et al.*, 1979; Borgono *et al.*, 1980; Southwick *et al.*, 1981; Cebrian *et al.*, 1983; Huang *et al.*, 1985; Chakraborty and Saha, 1987; Mazumber *et al.*, 1988; Bickley and Papa, 1989; Piontek *et al.*, 1989; Shannon and Strayer, 1989; Wu *et al.*, 1989; Engel and Smith, 1994; Chen *et al.*, 1996; Luo *et al.*, 1997; Mazumder *et al.*, 1997), as well as inhalation exposures (Perry *et al.*, 1948; Axelson *et al.*, 1978; Wall, 1980; Lee-Feldstein, 1983; Lagerkvist *et al.*, 1986, 1988; Beckett *et al.*, 1986; Bolla-Wilson and Bleecker, 1987; Ide and Bullough, 1988; Morton and Caron, 1989; Järup *et al.*, 1989). Cardiovascular effects attributed to chronic arsenic exposure included Blackfoot disease, arterial thickening, Raynaud's disease, ischemic heart disease and thrombosis; in several epidemiological studies, increased mortality due to cardiovascular disease was reported. Hepatic effects included hepatomegaly, portal fibrosis and hypertension, bleeding from esophageal varices; central and vascular fibrosis; cirrhosis, ascites, and fatty liver. Other effects included melanosis, keratosis, hyperkeratosis; hypo- and hyperpigmentation, pigmentation changes, warts, and gastrointestinal irritation.

Neurotoxic impacts observed in humans following subchronic and chronic exposure to arsenic *via* ingestion include impacts on both the sensory and motor nerves, typified as having only slow and generally incomplete recovery following cessation of exposure (Le Quesene and McLeod, 1977; Murphy *et al.*, 1981; Fincher and Koerker, 1987; Kiburn, 1997). Symptoms have been reported to include muscular weakness, paresthesia (of the limbs and extremities, ranging from numbness to prickling sensation), electromyographic abnormalities, functional denervation, mild peripheral neuropathy, and neurobehavioural abnormalities.

Histologically, neurotoxic impacts are manifested as a dying-back axonopathy with demyelination (Hindmarsh and McCurdy, 1986; Goebel *et al.*, 1990).

It has been suggested that chronic arsenic exposure may result in induction of diabetes mellitus, based on epidemiological studies of exposure *via* drinking water (Lai *et al.*, 1994), and *via* air in the workplace (Rahman and Axelson, 1995). Although no evidence of abnormalities in cell-mediated immunity was observed in an occupational epidemiology study, exposure levels were not determined (Bencko *et al.*, 1988).

The NOAEL for the effects discussed above in humans following chronic oral arsenic exposure was 0.006 mg As/kg body weight/day for populations exposed to arsenic in their drinking water (Southwick *et al.*, 1981); while the LOAEL (abnormal pigmentation) was 0.01 mg As/kg body weight/day in humans exposed to arsenic in their drinking water for 11 to 15 years (Borgono *et al.*, 1980). The chronic inhalation data did not support the selection of a NOAEL, while the lowest LOAEL (Reynaud's disease) was 0.05 mg As/m^3 in occupational workers exposed for 14 to 40 years (Lagerkvist *et al.*, 1986, 1988).

Occupational exposures to arsenic dusts have indicated that arsenic has the potential to cause contact dermatitis (typified by erythema and swelling, while papules and vesicles occurring in more severe cases) (Holmqvist, 1951; Pinto and McGill, 1953). These studies, in combination with the animal studies, suggest that the induction of dermatitis is likely limited to relatively high concentrations (ATSDR, 1993). Studies of dermal sensitization *via* patch tests (Holmqvist, 1951; Wahlberg and Boman, 1986), have yielded mixed results. ATSDR (1993) concluded that the relevance of the positive result to typical environmental exposures was doubtful.

4.2.2.2 Reproductive and Developmental Toxicity

4.2.2.2.1 Animal Studies

Reproductive toxicity is the occurrence of adverse effects on the reproductive system; and developmental toxicity is the occurrence of adverse effects on the developing organism resulting from exposure to a chemical prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation.

Many reproductive and developmental studies have been conducted to assess the effects of arsenic on laboratory animals and their offspring, and the majority of these studies have been conducted with parenteral administration. These studies have shown that intravenous and intraperitoneal administration of inorganic arsenic has been associated with fetal resorption, delayed growth and developmental malformations (primarily of the central nervous system, but also of the eye, skeleton, kidney and/or gonads) in hamsters, mice and rats (*e.g.*, Ferm and Carpenter, 1968; Ferm and Kilham, 1977; Hood *et al.*, 1977, 1978; Hood and Harrison, 1982; Willhite and Ferm, 1984; Ferm and Hanlon, 1986; Carpenter, 1987; Mason *et al.*, 1989; Domingo *et al.*, 1992). Statistical analyses have indicated a NOAEL of 2.5 mg As/kg, based

on hamsters dosed on gestational days 8, 11 or 12 (Hood and Harrison, 1982) and a LOAEL of 5 mg As/kg, based on several studies. The effects reported to result from parenteral administration are supported by the results of *in vitro* studies of the developmental impacts of arsenic. Growth retardation, developmental abnormalities and fetotoxicity were reported to be treatment-related effects following incubation of post-implanted mouse embryos with sodium arsenite and arsenate (Chaineau *et al.*, 1990). Tabacova *et al.* (1996) conducted an *in vitro* study of the effects of arsenate and arsenite in whole mouse embryo culture. Based on ED_{50} values for growth, development and malformation (consisting of neural abnormalities such as cranial neural tube non-closure), arsenite (As[V]) was about three-fold more potent than arsenate (As[III]). Tobacova *et al.* (1996) observed a decreasing susceptibility to neural tube defects with increasing gestational age of embryos. Data on the rates of neural tube defects in cultured whole embryos were interpreted by Tabacova *et al.* (1997) as indicating a possible oxidative damage mechanism of action for this effect.

The severity of developmental toxicity of arsenic in animals exposed *via* oral and inhalation routes differs significantly from that following parenteral administration. While oral and inhalation studies have indicated increased fetal resorptions and/or decreased offspring survival in rabbits, hamsters and mice, these effects were accompanied by maternal toxicity, and were not accompanied by significant increases in the occurrence of fetal malformations (Baxley *et al.*, 1981; Willhite, 1981; Kamkin, 1982; Hood and Harrison, 1982; WIL Research Laboratories, 1988a,b; Hood *et al.*, 1998). In rats, exposure to arsenic *via* oral or inhalation exposure did not result in adverse embryonic effects, neither resorptions or teratogenicity was observed in several studies (Kojima, 1974; Hood *et al.*, 1977; Stump *et al.*, 1998a,b). A few studies indicated increased rate of malformations in mice (Hood *et al.*, 1978; Nagymajtényi *et al.*, 1985) and delayed neurological development in pups (Earnest and Hood, 1981) following oral or inhalation exposure, but no data was available regarding maternal toxicity in these studies, and therefore the role of maternal toxicity in the occurrence of these effects cannot be ruled out. Colomina *et al.* (1996) observed that concomitant maternal exposure to arsenic and maternal stress (induced by restraint) resulted in an increase in fetal malformations, but neither treatment alone caused malformations.

Minimal or no developmental effects have been reported in offspring of animals exposed chronically to arsenic *via* oral administration. Schroeder and Mitchener (1971) observed no significant effects in mice exposed to 1 mg As/kg body weight/day, as sodium arsenite, *via* drinking water for 3 generations. Similarly, no effects were reported for the offspring of rats treated chronically *via* gastric intubation (Nadeenko *et al.*, 1978). At much higher doses, severe maternal and fetal toxicity (indicated by decreased body weights and reduced survival) was observed in mice administered arsenic acid in the diet for 2 generations (Hazleton Laboratories, 1990). Maternal and fetal NOAELs were reported to be 100 and 20 mg As/kg body weight/day, respectively.

Hood (1998) investigated the toxicity of organic arsenic (DMA), and based on the extreme doses required for fetal toxicity, concluded that any prenatal toxicity observed following

exposure to inorganic arsenicals is due to either direct or maternally-mediated effects of the parent compound, rather than to effects of the methylated metabolites.

4.2.2.2.2 Human Studies

The reproductive and developmental toxicity database in humans is limited and inconclusive (Goldman and Dacre, 1991; DeSesso *et al.*, 1998). Case-control epidemiological studies have indicated increased rates of spontaneous abortion, reduced birth weights and congenital malformations in the children of women working in or residing near smelter operations (Nordstrom *et al.*, 1978a,b, 1979a,b; Aschengrau *et al*, 1989; Börzsönyi *et al.*, 1992). DeSesso *et al.* (1998) cited the limitations of these studies as including: marginal increase in odds ratio, and inclusion of unity in the 95th percentile confidence interval indicating questionable causality of association between the proposed effects and arsenic exposure (Aschengrau *et al.,* 1989). DeSesso *et al.* (1998) also noted limitations in the human reproductive studies, including: uncertainty regarding exposure and lack of control of confounding factors Nordstrom *et al.* (1978a,b, 1979a,b); Börzsönyi *et al.* (1992). Ihrig *et al.* (1998) reported similar magnitudes of findings in of moderate- and high-exposure groups of women dwelling near a facility producing arsenic-based pesticides. Differences in incidences of stillbirth between various ethnic groups led Ihrig *et al.* (1998) to conclude that differential susceptibilities may be related to a genetic polymorphism affecting the metabolism of folate. DeSesso *et al.* (1998) reviewed this study, and concluded that confounding factors, such as prenatal care, may have affected the correlation, in that lower socioeconomic classes were associated with higher exposures. Zierler *et al.* (1988) reported that while there was no overall causal association between exposure in drinking water and congenital heart defects; a possible association between exposure and incidence of coarctation of the aorta was noted. However, given uncertainties in determination of exposure levels, it was concluded that this correlation was not indicative of arsenic being a causative agent of teratogenicity.

In contrast to the studies cited above where limited possible associated effects were noted, Concha *et al.* (1998b,c) reported that there were no adverse reproductive or developmental effects associated with high chronic arsenic exposure in a native Andean population. A common limitation to these epidemiological studies is the lack of sufficient information on the possible exposure to other chemicals, and uncertainties regarding determination of maternal exposures during critical periods of development (DeSesso *et al.*, 1998; Golub *et al.*, 1998).

DeSesso *et al.* (1998) conducted a comprehensive review of the embryotoxicity and teratogenicity of arsenic compounds in both humans and experimental animals, and concluded that the impact of arsenic on the developing fetus is greatly dependent on the route of exposure. These authors concluded that only under intravenous or intraperitoneal administration would the "extreme" concentrations required for teratogenic effects be achievable. They further concluded that because oral and inhalation studies have consistently shown a lack of dose-related teratogenicity, especially in studies compliant with Good Laboratory Practices, arsenic is unlikely to result in teratogenic effects in humans under

typical environmental exposure situations. In a review of the same database, Golub (1994) noted that maternal and developmental toxicity occur in the same dose range; however, these authors considered the developmental effects not to be secondary to maternal toxicity, based on the *in vitro* database, and *in vivo* data showing fetal toxicity in the absence of maternal toxicity (the studies to which they refer here were not specified). This review was re-visited in Golub *et al.* (1998), who attributed the differences in oral/inhalation studies and intravenous studies to differences in concentrations reaching the fetus. These authors characterized the main manifestation of the reproductive toxicity of arsenic as being detrimental impacts on development, resulting in a characteristic profile of malformations, growth retardation, and prenatal death; it was further concluded that environmental exposures could pose a risk to the fetus.

4.2.2.3 Genotoxicity

4.2.2.3.1 In Vitro - Bacterial Systems

There is a limited number of studies of the mutagenicity of arsenic in bacterial systems. Negative results were reported for arsenate and arsenite (Lofroth and Ames, 1978) in *Salmonella typhimurium* assays, without metabolic activation. Studies using *Escherichia coli* have yielded both positive (Nishioka, 1975) and negative (Rossman *et al.*, 1980) results for arsenite, although Rossman *et al.* (1980) identified several limitations in the earlier study, which render the significance of the positive result questionable. Yamanaka *et al.* (1989b) reported positive results in *E. coli* in the presence of oxygen. Ulitzer and Barrak (1988) treated *Photobacterium fischeri* with As(III) and As(V), and reported negative and positive results, respectively, for gene mutation.

4.2.2.3.2 In Vitro - Mammalian Systems

Several short-term *in vitro* genotoxicity assays in mammalian systems have indicated mixed results. Arsenic compounds were observed to induce sister chromatid exchange and chromosomal aberrations in hamster embryo cells (Larramendy *et al.*, 1981), mouse cells (Andersen, 1983; Moore *et al.*, 1997a), Chinese hamster ovary cells (Ohno *et al.*, 1982; Wan *et al.* 1982; Kochhar *et al.*, 1996) hamster-human hybrid cell lines (Hei *et al.*, 1998) and human lymphocytes, lymphoblasts and fibroblasts (Petres and Hundeiker, 1968; Paton and Allison, 1972; Larramendy *et al.*, 1981; Nakamuro and Sayato, 1981; Nordenson *et al.*, 1981; Wan *et al.* 1982; Andersen, 1983; Crossen, 1983; Jha *et al.* 1992; Oya-Ohta *et al.*, 1996; Iwami *et al.*, 1997; Rasmussen and Menzel, 1997). Arsenic was also observed to result in cell morphological transformations and DNA amplification in Syrian hamster embryo cells (Lee *et al.*, 1985, 1988; Barrett *et al.*, 1988). It was observed that arsenic induced chromosomal aberrations and SCEs during DNA replication, whereas in the absence of replication, no effects have been observed (Nordenson *et al.*, 1981; Crossen, 1983).

Negative results were reported for mutations, and specifically point mutations, in both mouse (Amacher and Paillet, 1980) and Chinese or Syrian hamster ovary (Rossman *et al.*, 1980, Lee

et al., 1985; Li and Rossman, 1991) test systems, and for sister chromatid exchange in mouse P388 cells (Andersen, 1983). In a time- and dose-related manner, inorganic arsenic was reported to both stimulate (at lower doses) and inhibit (at higher doses) DNA synthesis in human lymphocytes exposed *in vitro* (Meng, 1994). Iwami *et al.* (1997) observed that the organic metabolites of arsenic (DMA, MMA) were capable of inducing mitotic arrest and aneuploidy in cultured human lymphocytes. DMA was of greater potency with regard to aneuploidy, and was suggested to cause this effect through spindle disruption, as demonstrated by Ramirez *et al.* (1997).

A dose-related inhibition of lymphocyte proliferation was observed *in vitro* with cultured non-smoker and drug-free male and female human lymphocytes exposed to sodium arsenate or sodium arsenite (Gonsebatt *et al.*, 1992). A time-related decrease in lymphocyte proliferation was observed for all exposure durations in human lymphocytes cultivated with arsenic in the presence and absence of the lymphocyte proliferation stimulator phytohaemagglutinin (PHA)

Several authors have indicated that different arsenic species have varying mutagenic potencies in *in vitro* mammalian systems. Kochhar *et al.* (1996) observed that arsenite (As[III]) had greater potency than did arsenate (As[V]) in inducing chromosomal aberrations and sister chromatid exchanges in mammalian cells. Similarly, Moore *et al.* (1997a) reported that arsenite had the lowest effective doses in the L5178/TK$^{+/-}$ assay, followed by arsenate, MMA and DMA. Oya-Ohta *et al.* (1996) compared the mutagenic strength of several arsenic compounds, and determined that the strongest compounds, in terms of clastogenic potency (causing chromatid gaps and breaks), was arsenite (As[III]) followed, in order, by arsenate (As[V]), DMA, MMA, and TMA. In further examination of this issue, these authors observed that depletion of cellular glutathione (GSH) increased the incidence of chromosome aberrations induced by arsenite, arsenate, and MMA, while markedly suppressing the clastogenic effects of DMA.

Hei *et al.* (1998) studied the mutagenicity of arsenite in the hamster-human hybrid cell assay, and observed a significant reduction in the activity of arsenite when the cells were also treated with a oxygen radical scavenger. The authors concluded that the mutagenicity of arsenic is dependent on a reactive oxygen species, and that this might explain some of the differences observed between *in vitro* and *in vivo* assays.

4.2.2.3.3 In Vivo - Mammalian Systems

Studies of the mutagenicity of arsenic in *in vivo* mammalian systems have yielded mixed results. While Datta *et al.* (1996) reported increased chromosomal aberrations in rat bone marrow cells following oral exposure to As(V), weakly positive (Nagymajtényi *et al.*, 1985) or negative (Poma *et al.*, 1987) results have been reported for various cell types of the mouse following oral or inhalation exposure to As(III). Intraperitoneal administration of arsenic to mice has yielded negative results for chromosomal aberrations in bone marrow cells, spermatogonia, dominant lethal mutation, and sperm morphology (Deknudt *et al.*, 1986;

Poma *et al.*, 1987), while positive results were reported for micronuclei in bone marrow cells (Poma *et al.*, 1987; Tinwell *et al.*, 1991). Yamanaka *et al.* (1989a,b; 1991; 1995; 1996) reported that oral administration of DMA to mice at high doses resulted in DNA strand breaks or DNA-protein cross-links in the lungs. Similarly, Brown *et al.* (1997b) reported the induction of DNA damage in the lungs of rats following oral administration of DMA.

Following inhalation or oral exposure of human populations, there have similarly been mixed results with regards to the incidence of genetic alterations. A lack of chromosomal aberrations or in peripheral lymphocytes following oral exposure was reported (Burgdorf *et al.*, 1977; Vig *et al.*, 1984), while other authors (Nordenson *et al.*, 1978, 1979; Gonsebatt *et al.*, 1997) have observed increases in chromosomal aberrations in lymphocytes following oral and inhalation exposure. Both positive (Burgdorf *et al.*, 1977; Lerda, 1994) and negative results (Vig *et al.*, 1984) have been reported for sister chromatid exchanges in the lymphocytes of humans orally exposed to arsenic.

Rudel *et al.* (1996) discussed the issue of the relevance of the mutagenicity of arsenic species in the cell types described above to evaluation of human carcinogenicity, for which blood cells are not a target. Of potential relevance to the induction of bladder cancer is the prevalence of micronuclei in the exfoliated bladder cells of a population exposed to arsenic *via* drinking water. It was observed that the incidence of micronuclei increased with urinary speciated arsenic concentrations in a dose-dependent manner (Warner *et al.*, 1994; Gonsebatt *et al.*, 1997; Moore *et al.*, 1997b). Background or baseline urinary speciated arsenic concentrations in these studies were 34 and 59 µg As/L (Gonsebatt *et al.*, 1997; Moore *et al.*, 1997b, respectively), while the concentrations in the urine of exposed populations were 740 and 54 to 729 µg As/L, respectively. An exception to the dose-response was observed by Moore *et al.* (1997b), who reported that the group with maximum urinary levels (729 to 1894 µg As/L) had an incidence of micronuclei similar to the baseline, presumably as a result of toxic action of arsenic on the cells. Based on these results, the authors concluded that arsenic is clastogenic, and possibly weakly aneuploidogenic.

In a review of the mutagenicity database for arsenic, Rudel *et al.* (1996) noted the limitations of attempting to interpret the mutagenicity database with regard to establishment of a dose-response relationship and relevance to human carcinogenicity. These include the mixed results of *in vivo* studies of the ability of arsenic to induce genetic alterations, as well as lack of quantified exposure levels in epidemiological studies.

4.2.2.4 Carcinogenicity

4.2.2.4.1 Animal Studies

The experimental animal database for the carcinogenicity of arsenic compounds is limited, and is generally considered inadequate, and without consistent demonstration of carcinogenic activity (IARC, 1980; U.S. EPA, 1998). In a carcinogenicity study conducted by Kanisawa and Schroeder (1967), no increase in tumour incidence was observed in rats or mice

administered sodium arsenite or sodium arsenate in drinking water over their lifespan. Similarly, there was no evidence of carcinogenicity was observed in a group of mice exposed by inhalation to an aqueous aerosol of sodium arsenite (Berteau *et al.*, 1978). Both of these studies were deemed inadequate due to the fact that a single exposure concentration was employed, precluding their use in determining the carcinogenic potency of arsenic. Several other authors also reported a lack of carcinogenicity in animal studies, following oral exposure (Byron *et al.*, 1967; Schroeder *et al.*, 1968; Kroes *et al.*, 1974). Arsenic was also shown to lack activity as a promoter of tumorigenesis in mice, following dermal exposure (Kurokawa *et al.*, 1989) . However, an association between intratracheal instillation and increased frequencies of lung adenomas or carcinomas has been reported (Ishinishi *et al.*, 1983; Pershagen and Bjorklund, 1985; Yamamoto *et al.*, 1987).

4.2.2.4.2 Human Studies - Inhalation

The epidemiological literature has indicated a positive association between inhalation exposure to arsenic and lung cancer rates, in copper smelter workers exposed mainly to arsenic trioxide (Pinto *et al.*, 1977, 1978; Axelson *et al.*, 1978; Wall, 1980; Enterline and Marsh, 1982; Welch *et al.*, 1982; Lee-Feldstein, 1983; Enterline *et al.*, 1987; Järup *et al.*, 1989), in chemical plant workers exposed to arsenate (Ott *et al.*, 1974; Mabuchi *et al.*, 1979; Sobel *et al.*, 1988), and in residents near copper smelters or chemical plants using arsenic compounds (Matanoski *et al.*, 1981; Cordier *et al.*, 1983; Brown *et al.*, 1984; Pershagen, 1985).

The U.S. EPA has concluded that arsenic is a human carcinogen based on epidemiological evidence of respiratory cancer in workers in the non-ferrous mining industry (U.S. EPA, 1984a,b; 1998). Four reports of increased mortality due to respiratory cancer in workers in copper smelters were used by the U.S. EPA to derive 4 unit cancer risk estimates. In addition, unit risk estimates for arsenic exposure through drinking water have also been calculated. Each of these reports have been summarized below.

One of the 4 studies used in the U.S. EPA assessment was cited as an unpublished report by Higgins *et al.* and was published Welch *et al.* (1982). A cohort of 1,800 workers in a copper smelter were used and 4 exposure groups were assigned. Exposure to sulphur dioxide (SO_2) and asbestos as well as smoking habits were not considered to confound the results of this assessment. A unit risk for mortality due to respiratory cancer of 4.90×10^{-3} $(\mu g\ As/m^3)^{-1}$ was estimated from the study using a linear model (U.S. EPA, 1984a). Using an average body weight of 70 kg, an average inhalation rate of 23 m^3/day and a lifetime risk of developing cancer equal to one-in-one million, an RsD of 0.000067 µg As/kg body weight/day was calculated.

A second study used in the U.S. EPA arsenic assessment (Brown and Chu, 1983a) involved a different cohort (a total of 8014 workers) from the same copper smelter studied by Welch *et al.* (1982). Workers were exposed to arsenic trioxide as well as other chemicals, including SO_2. Using the multistage model equation supplied by Brown and Chu (1983a,b,c), the U.S.

EPA calculated a unit risk for the low exposure group to be equal to 0.00125 $(\mu g\ As/m^3)^{-1}$ (U.S. EPA, 1984a). This was converted to an RsD of 0.00026 µg As/kg body weight/day, based on a lifetime risk of developing cancer equal to one-in-one million.

The original reference for the third study (Lee-Feldstein, 1983) used by the U.S. EPA could not be obtained. According to the U.S. EPA (1984a), a total of 8045 workers in a copper smelter was assigned to 1 of 5 cohorts on the basis of the duration of exposure. Since no quantitative arsenic concentrations were specified, the U.S. EPA used data supplied by Morris *et al.* (1974) who estimated arsenic airborne concentrations, based on 702 samples collected from 1943 to 1958. The unit risk derived by the U.S. EPA (1984a) from the Lee-Feldstein (1983) study was reported to be 0.0028 $(\mu g\ As/m^3)^{-1}$. Calculation of an RsD, at a lifetime risk of cancer development equal to one-in-one million, resulted in a value of 0.00012 µg As/kg body weight/day.

A study of 2802 men in a copper smelter in Tacoma, Washington (Enterline and Marsh, 1982) was used as the fourth study in the U.S. EPA risk assessment. Urinary concentrations showed a decreasing trend over time and a linear relationship between the urinary concentration of arsenic and atmospheric concentrations has been defined (Pinto *et al.*, 1976). Unit risks for deaths due to respiratory cancer were calculated from these data for incidences following both a 0- and a 10-year lag [0.00681 and 0.0076 $(\mu g\ As/m^3)^{-1}$, respectively]. The U.S. EPA (1984a) used both of these values in calculating the average unit risk, although the 10-year lag data is more relevant in light of the 20-year latent period of lung cancer (Doll and Peto, 1978). The 0-year and 10-year unit risks, using a lifetime risk of cancer development equal to one-in-one million, were converted to RsDs of 0.000048 and 0.000043 µg As/kg body weight/day, respectively.

In addition to the reports discussed by the U.S. EPA (1984a,b), another study examining a cohort (3916) of arsenic exposed smelter workers in Sweden was conducted (Järup *et al.*, 1989). When the entire cohort is considered, the results showed a positive dose response between cumulative arsenic exposure and the risk of lung cancer. Statistically significant increases in standardized mortality rates for lung cancer were reported among exposed workers with less than 10 years employment. Nevertheless, of 7 exposure categories, a dose-response relationship was only apparent in the 2 highest exposure groups. No relationship between cumulative SO_2 exposure and mortality from lung cancer was observed although the risk was increased for all exposure groups. In addition, no significant dose-response relationship between arsenic and mortality from cardiovascular or cerebrovascular disease occurred. Analysis of the best fitting model for the total cohort yielded a potency estimate of 0.000343 $(\mu g\ As/kg\ body\ weight/day)^{-1}$ and a corresponding unit risk of 0.0039 $(\mu g\ As/m^3)^{-1}$.

Individual problems with each of the 5 inhalation studies discussed above, and in some cases problems with the interpretation of the data, complicate the analysis even further. The study conducted by Welch *et al.* (1982) contained the fewest problems since the effects of smoking and exposure to 2 other chemicals were examined. However, the confounding effects of greater than normal concentrations of airborne dust and SO_2 are not clear, and the data were

not presented in such a way as to consider latent periods for lung cancer development. In the report by Brown and Chu (1983a), actual measured arsenic concentrations were not specified, and it was necessary to estimate exposure concentrations. Also, estimates could be made for only the "light" exposure group since workers in the other 2 categories may have been exposed to greater concentrations of arsenic, due to the nature of the cohort criteria. The data used from the third report (Lee-Feldstein, 1983) could not be verified since the original document could not be located and the source of exposure concentrations was not cited by the U.S. EPA (1984a). In the fourth reference (Enterline and Marsh, 1982), the duration of exposure could not be ascertained from the data supplied and therefore, the latency period of lung cancer could not be taken into account. Also, arsenic exposure was calculated and not derived from measured atmospheric concentrations. Finally, in the fifth study (Järup *et al.*, 1989), arsenic concentrations had to be estimated since actual measurements were not available. Although the contribution of SO_2 to lung cancer incidence was examined, actual air concentrations of this gas were not available and estimates were used.

Enterline *et al.* (1987) conducted a reanalysis of the Tacoma, Washington data. To assess airborne risk in this cohort, a relation between airborne concentrations of arsenic and measured urinary arsenic must be determined. In the original analysis (Enterline and Marsh, 1982), this was based on the equation reported by Pinto *et al.* (1976). A review of the basis for this equation revealed several problems leading to under-estimation of exposure, and thus over-estimation of the unit risk. Analysis of the data using improved exposure estimates demonstrated a stronger relationship between cancer and arsenic exposure. When the Enterline *et al.* (1987) exposure data were assessed using the Tacoma cohort, an excellent fit between arsenic exposure and cancer incidence was obtained (Viren and Silvers, 1994). Regression analysis also yielded potency and unit risk values of 1.13×10^{-7} (μg As/kg body weight/day)$^{-1}$ and 0.00128 (μg As/m^3)$^{-1}$. Enterline (1997) reported that in a re-analysis of the data including an additional 10 year follow-up period, a better fit was observed in the relationship between arsenic exposure and respiratory cancers. This author also commented on the difficulty in estimation of air concentrations based on urinary arsenic concentration, for example, due to the increased use of protective gear in high-exposure workers.

Subcohort analysis of the Swedish study also has been conducted (Viren and Silvers, 1994). The cohort was split into 2 groups; workers hired in 1940 or after, and those hired prior to 1940. In both cases, when the regression was forced to the null, a very poor model fit resulted; however, the statistical fit to the data was considered acceptable by U.S. EPA standards. Among workers hired prior to 1940 and on or after 1940, the resultant unit risk values were reported to be 0.0046 and 0.0017 (μg As/m^3)$^{-1}$, respectively. There was no statistical evidence of an association between arsenic exposure and lung cancer risk in those hired in/after 1940.

The serious limitations discussed above regarding the available epidemiological studies, particularly that mixed exposures occurred in all studies, result in many uncertainties when estimating an exposure limit from these studies. In addition, the available data indicated that while arsenic is not mutagenic, it may be clastogenic at extreme exposure concentrations

compared to those associated with environmental sources of arsenic (, 1984a,b). Therefore, if arsenic was the causal agent in the development of respiratory cancers, the mechanisms for such effects are not likely to involve effects of arsenic on genetic material. Nonetheless, the data suggest an increase in cancer risk is associated with inhalation exposure to high concentrations of inorganic arsenic.

4.2.2.4.3 Human Studies - Oral

The epidemiological literature, consisting of case-control studies, ecological cohort studies and retrospective analyses, indicates an association between oral exposure to arsenic (mainly *via* drinking water) and cancer incidence. The most sensitive target tissue is considered to be the skin, based on incidences of squamous cell carcinoma, basal cell carcinoma and intraepidermal carcinoma, but concerns are also indicated for internal cancers of the liver (angiosarcoma and carcinoma), the urogenital system (bladder, kidney, prostate), and the lung, including cancer of the nasal cavity (Tseng *et al.*, 1968; Zaldivar, 1974; Lander *et al.*, 1975; Tseng, 1977; WHO, 1981; Zaldivar *et al.*, 1981; Cebrian *et al.* (1983); Luchtrath, 1983; Chen *et al.*, 1985; 1986; 1988a,b,c, 1992; Brown *et al.*, 1989; Gibb and Chen, 1989; Tsuda *et al.*, 1989; 1995; Wu *et al.*, 1989; Chen and Wang, 1990; Bates *et al.*, 1995; Chen and Lin, 1994; Chiou *et al.*, 1995). Several of these are discussed in greater detail below. There are several studies of exposure *via* drinking water which have failed to observe a significant relationship between exposure and skin cancer incidence (Southwick *et al.*, 1983; Morton *et al.*, 1976; Wong *et al.*, 1992). Reasons for the absence of a significant relationship in these studies is not known; Abernathy *et al.* (1996) suggested that exposures may have been too low or of short durations, or the study designs may not have been sufficiently sensitive.

Tsuda *et al.* (1989) attempted to assess the carcinogenicity of ingested arsenic by conducting a retrospective cohort study on the mortality of Japanese residents (n=281) who had been exposed to arsenic contaminated drinking water. There was no significant difference in mortality among the entire cohort, although of the 53 deaths, 18 were a result of cancer. Death due to all causes, all types of cancers, respiratory tract cancer, liver cancer and cancer of the uterus were all significantly greater in the study population than the expected value based on standard mortality for Japan, although differences were not significant for low and medium exposure groups. When the cohorts were divided into smokers (including ex-smokers) and non-smokers, death due to all causes, all types of cancer, and respiratory tract cancer were significantly greater than expected for the high exposure group only. When mortality and the severity of arsenicism were examined, death due to all causes, all cancers, respiratory cancers, and cancer other than respiratory cancer in the severe "symptoms" group were in excess of the expected, as was death due to respiratory cancers in the mild "symptoms" group. The authors state that these results suggest that lung cancer may be associated with ingested arsenic. However, the analysis of groups divided by smoking patterns indicate that it is more likely that the increased incidence of lung cancer was attributable to smoking habits rather than exposure to arsenic. In addition, several shortcomings of this study (Tsuda *et al.*, 1989) have been recognized by the authors (smoking

habits, small sample size, and a short latency period of 5 years) which limited the significance of the findings. Similar findings were reported in a subsequent study of 113 residents using drinking water with concentrations greater than 1 mg arsenic/L (Tsuda *et al.*, 1995). Based on an estimated 5 year exposure in 1955 to 1959, elevated standard mortality rates were reported for all deaths, all cancers, lung cancer and urinary tract cancer. In examining the potentially confounding incidence of smoking in the cohort, the authors concluded that the cancer rates indicated a synergistic relationship between smoking and arsenic exposure.

Brown *et al.* (1989) conducted a dose-response analysis of the incidence of skin cancer from inorganic arsenic exposure through drinking water. The data used were from studies on Taiwanese populations exposed to high arsenic concentrations in drinking water and the analyses were compared with data on skin cancer incidence in Mexican populations exposed to arsenic through drinking water. The unit risk of skin cancer at an exposure of 1 µg As/kg body weight/day ranged from 0.0013 to 0.003 using a quadratic or linear mathematical model, respectively. These unit risk estimates were in general agreement with those estimated for the Mexican populations. Brown *et al.* (1989) noted that a variety of factors confound the overall interpretation of the data relating skin cancer and arsenic exposure through drinking water. First, arsenic intakes from sources other than drinking water were not considered. Second, case fatality for gangrene related to skin lesions was high. Third, potential confounding or modification effects by other chemicals in the drinking water was not assessed. Fourth, skin cancer was the only response considered in the risk analysis and cancers of various organs were also elevated in the populations studied.

Chen *et al.* (1992) examined the incidences of liver, lung, bladder, and kidney tumours in a Taiwanese population exposed to elevated arsenic concentrations in well water. The Armitage-Doll model was used to calculate age-specific mortality rates from cancer, and cancer potency indexes were determined for internal organs based on the excess lifetime risk of developing cancer from oral intake of 10 µg As/kg body weight/day of arsenic. Assuming a linear dose extrapolation curve, the lifetime risk at 10 µg As/kg body weight/day could be adjusted to determine an RsD at a one-in-one-million level of risk, yielding RsD values ranging from 0.00083 to 0.0024 µg As/kg body weight/day for males, and from 0.00059 to 0.0028 µg As/kg body weight/day for females. There are several confounding factors which had not been accounted for in the Chen *et al.* (1992) study, such as source of cancer mortality data, the assumptions regarding levels of exposure over a lifetime, and the presence of other chemicals (Byrd *et al.*, 1996). The U.S. EPA (1998) did not consider this study adequate for determination of a unit risk factor.

Another pair of studies of the effects of chronic population-level exposures to arsenic in well water was conducted by Tseng *et al.* (1968) and Tseng (1977). The U.S. EPA (1998) described this as a cross-sectional study of 40,000 Taiwanese who were chronically exposed to arsenic-contaminated drinking water, with comparisons to 7500 persons drinking water relatively free of arsenic. The results indicated an excess of skin cancer, as well as increased incidence of blackfoot disease, hyperpigmentation and keratosis, with possible vascular

problems. The U.S. EPA cites several weaknesses of this study, including poor nutrition in the study population, possible genetic susceptibility, potential exposures to arsenic from other sources, and possible bias in examiners. These will be discussed in greater detail in Section 4.2.2.4.5. However, the U.S. EPA (1998) used this study to derive an oral slope factor of 0.0015 (µg As/kg body weight/day)$^{-1}$, corresponding to a drinking water unit risk of $5x10^{-5}$ (µg As/L)$^{-1}$.

Chiou *et al.* (1995) studied the incidence of cancers in 263 Blackfoot disease patients in a region of endemic arseniasis in Taiwan, in comparison to a group of 2,293 healthy people. Using Cox's proportional hazards regression analysis, a significant relationship was observed between arsenic exposure and cancers of the lung and bladder, as well as cancers of all sites, when age, sex and smoking status was controlled. The authors reported that both Blackfoot disease and smoking were associated with an increased incidence of cancer, after adjustment for cumulative arsenic exposure.

An ecological study of the incidences of cancer in the Taiwanese population of 243 townships, in relation to drinking water concentrations was conducted by Guo *et al.* (1997). Age, smoking and "urbanization" were controlled for in this study. A positive association was reported for exposure to water with high arsenic concentrations and transitional cell carcinomas of the bladder, kidney, and ureter, all urethral cancer combined, and adenocarcinomas of the bladder (males only). An association between the urbanization index and transitional cell carcinomas was also observed. Guo *et al.* (1997) interpreted the results as indicated arsenic may induce cell type-specific carcinogenicity.

In a case-control study, Bates *et al.* (1995) did not find an overall association of inorganic arsenic in drinking water (up to 160 µg As/L) with risk of bladder cancer in populations in Utah. The incidence of bladder cancer in the smoking sub-population of the exposure group indicated a positive trend; this was interpreted as supporting the findings of other studies of synergism between smoking and arsenic exposure. The lack of a correlation between arsenic exposure and cancer in this study is in disagreement with the studies cited above, and specifically, the use of the Tseng *et al.* (1968) and Tseng (1977) studies for development of a cancer risk estimate would overestimate the incidence of cancer in the Utah population. The authors suggested that this discrepancy may be due to bias in exposure estimation or simply due to chance.

Hsueh *et al.* (1995) observed a significant dose-response relationship between skin cancer prevalence and chronic arsenic exposure in residents in Taiwanese villages in which arseniasis was hyperendemic. Exposure was indexed by duration of residence in the area, duration of consumption of high-arsenic artesian well water, average arsenic exposure, and cumulative arsenic exposure. The overall prevalence of skin cancer was as high as 6.1%, showing an increase with age. In an evaluation of risk factors for skin cancer, it was observed that chronic carriers of hepatitis B surface antigen with liver dysfunction had an increased prevalence. Similarly, malnourishment, indexed by a high consumption of dried

sweet potato as a staple food, was also significantly associated with an increased prevalence of arsenic-induced skin cancer (Hsueh *et al.*,1995).

4.2.2.4.4 Mechanism of Action

4.2.2.4.4.1 Role of Arsenic in Carcinogenicity

Non-carcinogenic toxicity is attributed to interactions of inorganic arsenic, specifically As(III), with various tissues in the body. This conclusion is based on the observation of significant toxicity following exposure to inorganic arsenic species only (Vahter and Marafante, 1988), and is widely held to be true. In contrast, the determination of the arsenic species responsible for the carcinogenic activity associated with this metal is a matter of some dispute, partially related to the fact that the mechanism of carcinogenic action of arsenic has not been determined.

No clear picture of ranking potency of the different arsenic species emerges from the genotoxicity database. While studies of the *in vitro* clastogenicity of arsenic species indicated inorganic forms to have greater potency (Kochhar *et al.*, 1996; Oya-Ohta *et al.*, 1996; Moore *et al.*, 1997a), the database indicates that both inorganic and organic species are capable of inducing chromosomal aberrations.

Studies of various arsenic species have yielded mixed results with regard to induction of DNA damage, which can be considered to be indicative of cancer initiation. Following oral gavage to rats, neither arsenite nor arsenate resulted in DNA damage (Brown *et al.*, 1997b). Yamanaka *et al.* (1989a,b; 1991; 1995; 1996) reported that oral administration of DMA to mice at high doses resulted in DNA strand breaks or DNA-protein cross-links in the lungs. Similarly, Brown *et al.* (1997b) reported the induction of DNA damage in the lungs of rats following oral administration of DMA, even at more moderate dose levels. This DNA damage was attributed to production of dimethylarsenic peroxyl radicals, hydroxyl radicals and superoxide radicals (Yamanaka *et al.*, 1989a,b).

DMA has been reported to act as a promoter of carcinogenicity, based on enhanced tumorigenesis in the kidney, bladder, liver, thyroid gland, and lung (Shirachi *et al.*, 1983; Murai *et al.*, 1993; Yamanaka *et al.*, 1995; Yamamoto *et al.*, 1995; Wanibuchi *et al.*, 1996). Following oral administration to rats, sodium arsenite was observed to increase hepatic ornithine decarboxylase (ODC), a marker for promotion of carcinogenesis, and hepatic heme oxygenase activity, an indicator of changes in cell redox potential (Brown and Kitchin, 1996). In a similar study, Brown *et al.* (1997b) studied the impact of sodium arsenate, MMA and DMA on 6 biochemical parameters. DMA and MMA were reported to cause a decrease in alanine aminotransferase and glutathione, and an increase in cytochrome p450 content (also a marker for promotion of carcinogenicity), and DMA also caused a decrease in ODC. Arsenate had no effect on the biochemical markers for cancer promotion. Based on these findings, Brown *et al.* (1997b) suggested that DMA is an active promoter of multistage carcinogenesis, while As(III) also shows some evidence of promotion capability.

It has been proposed that arsenic may act as a comutagen, cocarcinogen or progressor (Barrett *et al.*, 1988; Chan and Huff, 1997). Brown and Chu (1983c) proposed that arsenic is a late-stage carcinogen, acting during progression, after completion of initiation and promotion by other causal agents, and before malignant cells are detectable. The role of arsenic as a progressor may be related to its impacts on gene amplification and cell proliferation, which would function to promote the proliferation and growth of transformed cells (Chan and Huff, 1997). It has been proposed that arsenic could enhance DNA damage or enhance inhibition of DNA repair processes of such agents as ultraviolet radiation or alkylating agents (Chan and Huff, 1997; Wiencke *et al.*, 1997; Yager and Wiencke, 1997). Based on the results of epidemiological studies, smoking has been reported to potentiate arsenic carcinogenicity (Pershagen, 1985; Bates *et al.*, 1995; Chiou *et al.*, 1995; Tsuda *et al.*, 1995). Administration of arsenic has been reported to enhance tumour growth and to decrease latency in mice (Schrauzer and Ishmael, 1974; Kerkvliet *et al.*, 1980; Shirachi *et al.*, 1983; Yamamoto *et al.*, 1995), and to transform benign tumour cells to malignant tumour cells (Barrett and Lee, 1992).

4.2.2.4.4.2 Theories on Mechanism of Action

Perturbation of Normal Methylation Processes

As discussed in Section 1.3, the primary metabolic fate of inorganic arsenic entering the body is methylation. Independent of species-specific toxic potency, and the effects of methylation on tissue concentrations of inorganic arsenic versus MMA and DMA, the process of methylation itself, and disturbance of the normal balance of methyl donors and receptors, has been proposed to have significant effects which could lead to genetic damage and carcinogenicity (Mass and Wang, 1997a).

Several studies have noted alterations in normal patterns of methylation following exposure to arsenic. Mass and Wang (1997b) reported hypermethylation (increased methylation) of cytosines in the region of the p53 tumour suppressor gene in a human adenocarcinoma cell line in *in vitro* cell systems exposed to arsenic. Hypermethylation may affect gene expression, and has been reported to cause inhibition of certain genes, such as the p16 tumour suppression gene (Gonzalez-Zulueta *et al.*, 1995; Herman *et al.*, 1995). Hypermethylation of DNA was theorized to result from inhibition of methyltransferases, with subsequent decreases in use of the methyl donor, and overmethylation of native methylation substrates.

It has been postulated that with excessive arsenic exposures, the subsequent depletion of the methyl donor s-adenosylmethionine might cause a decrease in the methylation of DNA routinely undertaken in DNA repair activities (Chan and Huff, 1997; Mass and Wang, 1997b). The resultant hypomethylation of DNA due to the depleting effects of methyl donors by arsenic could lead to fragility of DNA and subsequent initiation or promotion of cancer. As other known hypomethylating agents are also clastogens [*e.g.*, 5-azacytidine, ethionine (Collins and Meyers, 1987; Perticone *et al.*, 1987; Meehan *et al.*, 1990)], this mechanism could lead to the DNA strand breakage observed by Yamanaka *et al.* (1989a,b).

If this mechanism has a role in arsenic carcinogenicity, then individual characteristics, such as methylation activity and nutritional status (*i.e.,* adequacy of the methyl donor pool) would affect individual susceptibility to arsenic. In addition, genetic polymorphism for methylation capacity, as has been reported in the human population related to ethnicity, age, and previous exposure status (Chappell *et al.,* 1997), could affect individual susceptibility to arsenic.

Incorporation into Native Enzymes or DNA

Chan and Huff (1997) suggested that due to its similarity to phosphate, arsenic (as As[V])could, by mis-identification as phosphate, become incorporated into DNA during replication. The resultant bond would be weaker than the normal phosphodiester bond, resulting in structural instability in the DNA. This effect would lead to the observed genotoxic endpoints attributed to arsenic (clastogenicity, chromosomal aberrations, sister chromatid exchange, and micronuclei formation). However, because As(V) is the form more similar to phosphate, and is the form which is incorporated in to bodily tissues based on this similarity (*e.g.*, into bones), this theory would not explain why As(III) is more active in inducing chromosomal aberrations than is As(V) (*e.g.,* Kochhar *et al.*, 1996; Moore *et al.*, 1997a; Oya-Ohta *et al.*, 1996).

Alternately, the similarity of arsenic to phosphate or sulphate may result in the incorporation of arsenic into enzymes, with subsequent impairment of normal enzyme activity (Chan and Huff, 1997). For example, Mitchell *et al.* (1971) suggested that arsenic may inhibit mitochondrial energy-linked functions through competition with phosphate during oxidative phosphorylation, thereby uncoupling the reaction, and by forming a complex with lipoic acid cofactors and subsequent inhibition of NAD-linked substrates, as has been observed by Crane and Lipmann (1953).

Trivalent arsenic is known to interact with tissues through binding to sulfhydryl groups (Vahter and Marafante, 1988), resulting in elevated concentrations in sulfhydryl-rich tissues such as hair and nails. This affinity may also result in the incorporation of arsenic into DNA or enzymes (Rudel *et al.,* 1996; Chan and Huff, 1997). Arsenic has been shown to inhibit DNA repair enzymes (*e.g.*, the ligase I and II enzymes), which contain essential sulfhydryl groups (Rudel *et al.*, 1996). Subsequent decreases in DNA repair might be responsible for DNA amplification and cell transformation (Rudel *et al.*, 1996). Experimental inhibition of the DNA repair enzymes, ligase I and II, has been shown to result in clastogenicity (Li and Rossman, 1989), a genotoxic effect associated with arsenic.

Lipid Peroxidation

Several investigators have demonstrated that DMA is capable of inducing DNA damage in lung tissue such as strand breaks or cross links (Yamanaka *et al.,* 1989a,b; 1991; 1995; 1996; Brown *et al.,* 1997b). It has been postulated that this damage is induced through active oxygen species (superoxide anion radicals and hydroxyl radicals) produced by the reaction of

molecular oxygen and dimethylarsine (a metabolite of DMA) (Chan and Huff, 1997). Such reactions could lead to the promotion of cancer by arsenic.

Gene Amplification/Expression

Through some of the mechanisms discussed above, arsenic has been shown to cause gene amplification and cell proliferation (Lee *et al.*, 1985; 1988). It has been postulated that in cases of arsenic-induced promotion, the genes upon which this activity is directed are involved in carcinogenicity (*e.g.*, oncogenes) (Barrett and Lee, 1992; Chan and Huff, 1997). This hypothesis is supported by the observation that oncogene expression has been reported to be amplified in human and animal tumours (Chan and Huff, 1997). Gene amplification could also lead to clastogenicity and malignant transformation through inhibition of DNA repair and stimulation of cell division (Rudel *et al.*, 1996; Chan and Huff, 1997). Rudel *et al.* (1996) specifically proposed a mechanism involving the induction of heat shock proteins (produced in every cell following stress [Welch and Suhan, 1986]) by arsenic exposure. Rudel *et al.* (1996) pointed out that at least 1 heat shock protein is involved with the gene(s) for certain DNA repair enzyme(s), and that perturbation of the heat shock protein could lead to amplification of that gene and thus to interference with normal DNA repair. Chan and Huff (1997) suggested that the formation of apurinic or apyrimidic sites in DNA as a result of disturbance of excision repair processes could lead to DNA single strand breaks and DNA protein cross-links.

Interaction with Other Chemicals through Concomitant Exposures

It has been proposed that arsenic may act as a comutagen, cocarcinogen, promoter or progressor, when individuals are exposed to arsenic at the same time as other chemicals capable of carcinogenic activity (Byrd *et al.*, 1996; Chan and Huff, 1997). It was thought that arsenic could enhance DNA damage through inhibition of DNA repair processes caused by such agents as ultraviolet radiation or alkylating agents (Chan and Huff, 1997; Wiencke *et al.*, 1997; Yager and Wiencke, 1997). The role of arsenic as a progressor may be related to its impacts on gene amplification and cell proliferation, which would function to promote the growth of transformed cells (Chan and Huff, 1997). Arsenic has also been reported to be capable of transformation of benign tumour cells to malignant tumour cells (Barrett and Lee, 1992). Byrd *et al.* (1996) suggested that populations might be exposed to arsenic and a proximal carcinogen whose concentrations correlated to that of arsenic, in this scenario, arsenic would act as a promoter of various tumour types. The dependence on co-exposure to an initiator of cancer was thought to provide a reason for the wide range of tissues-specific cancers with which arsenic has been associated.

Effects of Nutritional Status

In general, poor nutritional status can lead to increased susceptibility to the toxic action of many chemicals. In the case of arsenic, there may be an additional role of nutrition in

resistance or susceptibility to carcinogenicity. The methylation of arsenic following absorption has 2 general effects:

i) The conversion from inorganic species to MMA and DMA, with subsequent impacts on altered toxic potency; and,

ii) The impact on normal methylating activity in the body, especially of DNA and enzymes, as discussed above.

In addition, as stated earlier, As(III) has a high affinity for sulfhydryl groups; binding to such groups in DNA repair enzymes could lead to gene amplification. Alternately, binding to non-essential sulfhydryl groups, such as those provided in the diet, could provide a substitute for sulfhydryl binding of arsenic, thereby protecting the essential sulfhydryl groups. Therefore, the supply of sufficient levels of sulfhydryl groups and methyl donors (*e.g.*, proteins and amino acids such as cysteine and methionine), may play a significant role in susceptibility to arsenic carcinogenicity (Chan and Huff, 1997).

This theory is supported by several studies in the literature. Vahter and Marafante (1987) studied the impact of a methionine/cysteine reduced diet on the methylating activity of rabbits, and reported a significant decrease in methylation of inorganic arsenic following a 25% reduction in dietary intake of the amino acids. In an epidemiological study of cancer incidence in a Taiwanese village exposed *via* arsenic, Hsueh *et al.* (1995) found that malnutrition, indexed by a high consumption of dried sweet potato as a staple food, was a risk factor for skin cancer.

The importance of nutrition in maintaining adequate levels of methyl donors and sulfhydryl groups has been proposed as a reason for increased cancer risks in subsets of the Taiwanese population, in comparison to those observed in North American populations (and thus for the over-prediction of risks of skin cancer in North American populations exposed to arsenic in drinking water). However, Smith *et al.* (1995) reviewed the Taiwanese intake of protein, and found it adequate by current standards. Beck *et al.* (1995), in rebuttal, pointed out that current standards dictate intakes required for normal bodily processes, and may not be adequate to methylate an excessive and sustained intake of arsenic.

Other Possible Mechanisms

Burns *et al.* (1994) proposed that arsenic-induced immunosuppression may result in reduced natural immune surveillance, which would normally repair or remove transformed and damaged cells prior to tumourigenesis.

4.2.2.4.4.3 Toxicological Significance of the Threshold of Methylation Theory

As was discussed in Section 1.3.1.2, there has been considerable debate in the published literature regarding the existence of a threshold or saturation of methylation, that is, that there

are exposure levels above which the proportions of methylated species will be reduced. Such a mechanism for arsenic carcinogenicity would indicate a dose-response threshold, in that rates of exposure to arsenic below which methylation is saturated would not result in an increased risk of cancer. In addition, there is considerable evidence in the scientific literature regarding interindividual differences in basic methylation capacity, which has been related to age, gender, ethnicity, smoking, and previous arsenic exposure. The importance of such differences in methylation, in terms of evaluating the potential health effects, whether those occurring over different doses, or those occurring in different individuals, must be discussed in the context of the impacts on tissue interactions and toxic potencies of the various arsenic species.

Saturation of the methylation capacity would result in increased amounts of inorganic arsenic (As[III] or As[V]) and decreased amounts of MMA and DMA. Proponents of the methylation saturation theory have indicated that it is manifest by an increased urinary MMA:DMA ratio. The relationship of increased urinary MMA:DMA ratio to changes in species proportions in the body is not completely clear, that is, whether the concentrations of MMA in the body would also be elevated has not been determined. Therefore, the methylation saturation theory could imply that the body tissue concentrations of inorganic arsenic and/or MMA would increase, while concentrations of DMA would decrease. The next question is whether such a change would be a detoxification step or a toxification step.

Based on its affinity for sulfhydryl groups, trivalent arsenic (As[III]) has long been considered to be the primary form of arsenic interacting with bodily tissues, and thereby inducing the toxic effects associated with arsenic. The specific mechanism of action for this step is proposed to be an inhibition of mitochondrial energy-linked functions (*e.g.*, uncoupling of oxidative phosphorylation). Obviously, methylation would decrease this form of tissue interaction, and would then be considered a detoxification step.

However, while As(III) has shown some ability to act as a clastogen and possibly a promoter of carcinogenesis, DMA has demonstrated a capacity for both DNA damage and cancer promotion. While this does not confirm the species responsible for arsenic carcinogenicity, the theory regarding the role of methylation as a mechanism of detoxification may not be valid. If DMA is capable of initiating or promoting cancer, then the methylation of inorganic arsenic would actually be a toxification process.

4.2.2.4.5 Extrapolation from Cancer Risk Factors to Typical Environmental Exposures

As will be detailed in Section 4.2.2.5, the has derived cancer risk estimates for arsenic based on Tseng *et al.* (1968) and Tseng (1977) for oral exposure, and on the 4 occupational inhalation studies (Brown and Chu, 1983a,b,c; Lee-Feldstein, 1983; Higgins *et al.*, 1982; Enterline and Marsh, 1982), assuming a linear dose-response relationship. The application of these values to the estimation of risk to populations exposed to arsenic is thus dependent on the proper extrapolation from the high doses of the studies to much lower typical

environmental concentrations. Several epidemiological studies of exposure *via* drinking water or inhalation have failed to observe the expected incidence of cancers, leading to the questioning of the relevance of the cancer risk estimates to the low exposure scenarios. Their questionable relevance for application in a typical risk assessment is illustrated by Farago *et al.* (1997), who found no relationship between incidence of bladder cancer in southwest Wales and modelled multipathway exposures to arsenic *via* contaminated soils, dust and drinking water. Uncertainties in the studies forming the basis for the estimates, as well as several investigations into the applicability of the cancer risk estimates and the significance of the threshold of methylation hypothesis, are discussed below.

4.2.2.4.5.1 Uncertainties in Tseng *et al.* Studies

As the basis of the cancer slope factor, the studies by Tseng *et al.* (1968) and Tseng (1977) have come under a great deal of scrutiny. In general, criticisms relate to estimation of exposure, the nutritional status of the Taiwanese population, and the possibility of confounding factors such as concomitant exposure to other chemicals.

The selection of exposure groups based on average concentrations of arsenic in village wells is a source of uncertainty in these studies (Brown *et al.*, 1997a; Chappell *et al.*, 1997). Any one village was represented merely as the average well water concentration for the entire village, even though there was a large variation across all wells. This method not only prevents any ability to assess individual rates of exposure to those who developed cancers because of the lack of linkage with well water concentrations of arsenic, and well usage rates. In addition, Tseng *et al.* (1968) indicated that there was considerable variation in arsenic concentrations within wells over time, which was not addressed in the exposure estimation. These limitations are critical if the causality of cancer by arsenic is related to some saturable process (such as methylation) that would occur in people drinking well water with arsenic concentrations substantially greater than the average concentration. Brown *et al.* (1997a) interpreted the above limitations, together with the sensitivity of the cancer risk estimate to the model used and to uncertainties in exposure levels, as indicating that the Tseng *et al.* (1968) studies are not suitable for dose-response assessment, and for extrapolating to lower exposure levels.

The exposure estimation, and thus the cancer risk estimation, was based on the assumption that all of the exposure was derived from drinking water, when in fact, the diet and the environment may have provided significant additional sources (Brown and Abernathy, 1997; Chappell *et al.*, 1997). Brown and Abernathy (1997) concluded that the inclusion of dietary intake of arsenic in the cancer risk estimate would have significantly reduced the Maximum Likelihood Estimate. Mushak and Crocetti (1995) had also discussed this aspect of the Tseng *et al.* (1968) studies. Referring to work by Pyles and Woolson (1982) and the OMOE (Weiler, 1987), Mushak and Crocetti (1995) noted that proportions of inorganic arsenic species in vegetables, and specifically potatoes are less than 10%, meaning that dietary exposures to inorganic arsenic would likely be insignificant. Herbal medicines and teas,

however may represent a significant source of exposure to inorganic arsenic (Espinoza *et al.*, 1995; Ernst, 1998).

Concomitant exposures to other chemicals may be confounding factors in the Tseng *et al.* (1968) studies; Byrd *et al.* (1996) suggested that humic acids, for which elevated concentrations in drinking water are correlated to that of arsenic, may interfere with the cancer incidence due to arsenic alone. Chan and Huff (1997) also considered humic acid to be a potentially confounding factor in these studies, observing that humic acid is mutagenic and produces symptoms similar to those of blackfoot disease, although the occurrence of arsenic-related cancers has been reported in the absence of humic acid exposure.

The importance of nutritional status, as well as the actual nutritional status of the study population, has been debated in the literature. In general, poor nutritional status can lead to increased susceptibility to the toxic action of many chemicals. In the case of arsenic, there may be an additional role of nutrition in resistance or susceptibility to carcinogenicity. As was discussed in Section 4.2.2.4.4, the metabolism of arsenic following absorption, specifically methylation activity, has been postulated to play a role in the genotoxicity and carcinogenicity of arsenic, whether through conversion of As(III) to MMA and DMA, or through indirect impacts on DNA. Thus, the status of the methyl donor pool, which is dependent on dietary intake of proteins and amino acids such as cysteine and methionine, may play a significant role in susceptibility to arsenic carcinogenicity. Indeed, Hsueh *et al.* (1995) found that malnutrition, indexed by a high consumption of dried sweet potato as a staple food, was a risk factor for skin cancer. However, Smith *et al.* (1995) reviewed the Taiwanese intake of protein, and found it adequate by current standards. Beck *et al.* (1995), in rebuttal, pointed out that current standards dictate intakes required for normal bodily processes, and may not be adequate to methylate an excessive and sustained intake of arsenic.

4.2.2.4.5.2 Validation of the Dose-Response Curve at Low Exposure Rates

The rates of exposure in the studies which provide the bases for the cancer risk estimates are very high relative to the rates of exposures expected in most risk assessment situations related to general environmental exposures. Therefore, the validity of the use of this data in extrapolating cancer risks from high to low exposures assuming a linear dose-response curve (*i.e.*, that risk increases with exposure in a linear fashion) must be examined in order to validate use of these factors in risk assessment.

There are several studies of exposure *via* drinking water have failed to observe a significant relationship between exposure and skin cancer incidence (Southwick *et al.*, 1983; Morton *et al.*, 1976; Wong *et al.*, 1992; Bates *et al.*, 1995); however, these studies also suffer from deficiencies related to reliability of exposure estimations, population sizes, and the ever-present problem of attempting to prove a negative or lack of effect. The lack of a correlation between arsenic exposure and cancer in these studies is in disagreement with the studies of cancer incidence in populations experiencing higher exposures. These results can then be interpreted as indicating that the use of the Tseng *et al.* (1968) and Tseng (1977) studies for

development of a cancer risk estimate would overestimate the incidence of cancer in the study population. Although reasons for the absence of a significant relationship in these studies is not known, Abernathy *et al.* (1996) suggested that exposures may have been too low or of short durations, or the study designs may not have been sufficiently sensitive. Bates *et al.* (1995) suggested that this discrepancy may be due to bias in exposure estimation or simply due to chance. However, these studies may also be an indication that the extrapolation of cancer risks from the high exposures of Tseng *et al.* to low exposures is not valid.

Several authors have examined the dose-response curves of cancer incidence and exposure levels, in order to determine if the extrapolation of Tseng *et al.* (1968) is supported at low exposure levels. Rudel *et al.* (1996) reviewed genotoxicity studies in order to ascertain dose-response curves; it was concluded that for most endpoints (clastogenicity, chromosomal aberrations excepting sister chromatid exchange), there was a sublinear or threshold dose-response. Thus, it was concluded that use of a linear dose-response curve to extrapolate to low doses would overestimate risks.

Guo and Valberg (1997) examined the validity of the use of the cancer slope factor (CSF) in prediction of risks at low exposure levels. Using a likelihood analysis, the results of multiple epidemiological studies of skin cancer incidence and arsenic exposure *via* drinking water in countries around the world were analyzed. Guo and Valberg (1997) observed that at drinking water concentrations between 170 and 270 µg As/L, the CSF overestimated skin cancer risks. At concentrations under 170 µg As/L, the epidemiological data were concluded to be inadequate to evaluate the CSF. In support of the conclusion that the CSF overestimates cancer risks at low exposures, Guo and Valberg (1997) further reported that, even with a pooled sample size of 195,000, the statistical analysis was unable to detect a difference in cancer incidence in "exposed" populations (up to 270 µg As/L in drinking water) versus baseline cancer rates. In a similar analysis, Valberg *et al.* (1998) examined the results of 4 North American studies to evaluate the use of the CSF in extrapolation to low dose exposures. Again, the CSF was found to overpredict the incidence of skin cancer in populations exposed to less than 400 µg As/L. Valberg *et al.* (1998) noted several limitations which may have affected the outcome of this analysis, including: the assumption that individuals were exposed for a chronic duration, exposure was estimated at a population level, not an individual level, uncertainties in the measurement of arsenic in drinking water, and uncertainties with regard to age distributions (*i.e.,* the CSF best predicts cancer incidence in older age groups).

In contrast to the studies described above, Hertz-Picciotto and Smith (1993) observed that the dose-response curve for lung cancer risks associated with inhalation exposure to arsenic would indicate a supralinear dose-response curve. Based on a review of 6 occupational epidemiological studies, a steeper slope was observed in the low dose range, indicating that extrapolation from high dose to low dose would underestimate lung cancer risks. Several reasons were offered to explain this observation. Because occupational studies formed the basis for this evaluation, it is possible that at higher exposure levels, use of protective gear

would reduce actual exposure levels. This has also been postulated to be a potentially confounding factor in determination of exposure by Enterline (1997). Differences in types of exposures and forms of arsenic experienced at higher exposure levels may have affected absorption from the lung. Concomitant exposures to other potentially cancer-causing chemicals may have inflated the baseline cancer risk in some of the studies. Smoking has been proposed to have a synergistic effect on arsenic carcinogenicity, with a greater synergism at lower arsenic exposure levels (*e.g.*, at residential exposures as opposed to occupational exposures) (Pershagen, 1985), a disparity of cigarette use in the different study groups may have affected cancer rates. A final proposal for the observed dose-response curve was the "healthy worker effect" especially in the higher exposure groups. In order to evaluate this last factor, Arrighi and Hertz-Picciotti (1996) examined the effect of controlling for the healthy worker effect on cancer risk estimates. While controlling for healthy worker effect did not significantly affect the dose-response curve, such an analysis did yield stronger associations.

4.2.2.4.5.3 Consideration of Sensitive Subpopulations

There are, as discussed above, several theories as to the mechanism of action of arsenic which is responsible for its carcinogenic potency. These include incorporation into native proteins or DNA, lipid peroxidation, gene amplification, interaction with other chemicals, and nutritional status. Individual differences, whether resulting from genetically-based differences in biochemistry, nutritionally-based differences in metabolism, or from differences in concomitant chemical exposure profiles, could result in subpopulations of greater or lesser susceptibility to the toxic impacts of arsenic. For example, while the role of methylation as detoxification of inorganic arsenic is of some debate, there is evidence in the literature that indicates certain human subpopulations have varied capacities for arsenic methylation, dependent on ethnicity, age, gender, and smoking status.

4.2.2.5 Exposure Limits

Exposure limits derived by the U.S. EPA (1998) were selected for use in this assessment; however, the interpretation of the resultant risk estimates must consider the limitations of this exposure limit as discussed in the preceding sections of this report. The U.S. EPA derives exposure limits for both threshold and non-threshold effects when data is available. The Reference Dose (RfD) and Reference Concentration (RfC) are based on the assumption that a thresholds exist for certain toxic non-carcinogenic effects such as cellular necrosis. In general, the RfD (or RfC) is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

The U.S. EPA (1998) has classified arsenic as a Group A carcinogen (human carcinogen). The unit risk factor (or q_1^*) is based on the assumption that carcinogenic effects do not have a threshold (*i.e.*, dose-response relationship is linear).

4.2.2.5.1 Oral Exposure Limit

The U.S. EPA (1998) calculated an oral RfD of 0.3 µg As/kg body weight/day based on the epidemiological studies of chronic exposure to arsenic through drinking water (Tseng *et al.*, 1968; Tseng, 1977). Critical effects were hyperpigmentation, keratosis, and possible vascular complications at a lowest-observable-adverse-effects-level of 14 µg As/kg body weight/day. The RfD was based on a NOAEL of 0.8 µg As/kg body weight/day, with the application of an uncertainty factor of 3 to account for both lack of data on reproductive toxicity in humans, and for differences in individual sensitivity. The U.S. EPA (1998) noted some limitations of the studies, in that the exposure levels were not well-characterized and other contaminants were present. Health Canada (1996) has recommended a provisional tolerable daily intake (PTDI) of 2 µg As/kg body weight/day based on technical reports form annual meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA); however, this PTDI was not used in this assessment. For the purposes of the current assessment, the more conservative exposure limit, 0.3 µg As/kg body weight/day, was selected as the oral exposure limit for non-carcinogenic effects. If the information reviewed in the preceding sections of this report indicating that arsenic may be a threshold carcinogen are considered valid, then the exposure limit of 0.3 µg As/kg body weight/day would also be appropriate for the evaluation of the carcinogenic potential of arsenic exposures from specific environmental sources.

Arsenic exposure *via* the oral route was considered by the U.S. EPA to be carcinogenic to humans, based on the incidence of skin cancers in epidemiological studies examining human exposure through drinking water (Tseng *et al.*, 1968; Tseng, 1977). The researchers observed an increased incidence of skin cancer of the Taiwanese population which consumed arsenic-contaminated water. Based on the application of a linear-quadratic mathematical model to the data from these studies, the U.S. EPA (1998) calculated an oral q_1^* of 0.0015 (µg As/kg body weight/day)$^{-1}$. It was assumed that the Taiwanese individuals had a constant exposure from birth, and that males consumed 3.5 L drinking water per day, and females consumed 2.0 L per day. Doses were converted to equivalent doses for U.S. males and females based on differences in body weights and differences in water consumption and it was assumed that skin cancer risk in the U.S. population would be similar to the Taiwanese population. The multistage model with time was used to predict dose-specific and age-specific skin cancer prevalence rates associated with ingestion of inorganic arsenic; both linear and quadratic model fitting of the data were conducted. The q_1^* of 0.0015 (µg As/kg body weight/day)$^{-1}$, corresponding to an RsD of 0.00067 µg As/kg body weight/day for an acceptable risk level of one-in-one million, was adopted as the oral exposure limit for carcinogenic effects of arsenic for this assessment.

Recently, there has been concern on the part of regulators regarding the applicability of the arsenic cancer potency estimates for cancers at other sites (specifically bladder cancer) in setting exposure limits for arsenic. The National Research Council (NRC) (1999) has recently re-evaluated drinking water criteria for the United States, based on bladder cancer incidence data in the Taiwanese population as presented in Wu *et al.* (1989), Chen *et al.*

(1992) and Smith *et al.* (1992). NRC (1999) emphasized that the evaluation of cancer potency factors for bladder cancer has been limited by the amount and the quality of data available for use in the linear model. While the bladder cancer value would yield a greater cancer potency than that based on skin cancer, these data are still limited by many of the same problems as the potency factor for skin cancer, including large uncertainty of total daily exposure to inorganic arsenic (*i.e.*, the poor linkage between water concentrations of arsenic and individual exposure, and lack of data on arsenic intake from food), concomitant exposures to other chemicals and carcinogens (which would be especially important if arsenic is a cancer promoter), and differences in nutritional and health status between Taiwanese and North American populations. Because the intended use of the cancer potency factor is in the estimation of risk to a particular population in comparison to a "background" or "typical" population, and risks for both will be assessed with the same methodologies and the same exposure limit, the use of the skin cancer potency factor is considered acceptable and conservative.

4.2.2.5.2 Inhalation Exposure Limit

There were no regulatory guidelines for an inhalation exposure limit based on non-carcinogenic endpoints; therefore, the oral RfD, adjusted for bioavailability, was used to assess the non-carcinogenic effects of arsenic *via* inhalation. Similar to the discussion above, if the arguments that arsenic acts as a threshold carcinogen are accepted, the oral RfD, adjusted for bioavailability, would also be appropriate for assessing potential risks of cancer from inhalation exposure to arsenic.

The U.S. EPA (1998) considers arsenic to be a non-threshold carcinogen. Based on this assumption, the U.S. EPA (1998) calculated an inhalation q_1^* of 0.0043 $(\mu g\ As/m^3)^{-1}$, based on studies by Brown and Chu (1983a,b,c), Lee-Feldstein (1983), Higgins *et al.* (1982), and Enterline and Marsh (1982) which indicated increased lung cancer mortality of exposed populations. A geometric mean was obtained for data sets obtained with distinct exposed populations (Anaconda smelter and ASARCO smelter), and then the final estimate was the geometric mean of those 2 values. It was assumed that the increase in age-specific mortality rate of lung cancer was a function only of cumulative exposures. The q_1^* was converted to 0.013 $(\mu g\ As/kg\ body\ weight/day)^{-1}$ assuming a 70 kg adult breathes 23 m^3/day.

The Ontario Ministry of the Environment and Energy (OMEE, 1994) recommended a 24-h reference concentration of 0.3 $\mu g\ As/m^3$ (equivalent to 0.1 μg As/kg body weight/day assuming a 70 kg adult breathes 23 m^3/day); however, this acute exposure limit was not used in this assessment.

It has been suggested that because exposures to air-borne arsenic would be mediated by inhalation of particulate matter, and since a higher proportion of particulate matter would be respirable in occupational settings as compared to environmental exposures, the inhalation potency of arsenic based on occupational studies is likely overestimated for exposures associated with environmental contamination.

4.2.2.5.3 Dermal Exposure Limit

The U.S. EPA (1998) does not determine exposure limits for dermal exposure; therefore, the oral RfD and oral q_1^*, adjusted for bioavailability, were used to assess the non-carcinogenic and carcinogenic effects, respectively, *via* dermal exposure for this assessment. Again, if arsenic acts as threshold carcinogen, the oral RfD would be an appropriate exposure limit for the evaluation of carcinogenic risks from dermal arsenic exposure.

4.2.2.5.4 Bioavailability Values for Use in Assessment

Human bioavailability for arsenic was assumed to be 60 to 75% for ingestion; 30 to 34% for inhalation, and 0.8 to 1.9% for dermal exposure for this assessment.

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PART 4.3
TOXICOLOGICAL REVIEW: COBALT

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4.3.0 TOXICOLOGICAL REVIEW: COBALT

4.3.1 Fraction Absorbed *Via* Different Routes

4.3.1.1 Fraction Absorbed Via Ingestion

Dietary absorption of cobalt varies depending on its form and dose. Gastrointestinal absorption of cobalt in humans ranges from 18 to 97% of the administered dose depending on the size of the dose, the type of cobalt compound and the nutritional status of the subjects (Harp and Scoular, 1952; Valberg *et al.*, 1969; Sorbie *et al.*, 1971). When administered as an inorganic salt, cobalt absorption ranges from 1 to 44% (Carson *et al.*, 1987). Larger doses are absorbed less thoroughly than smaller doses (Stokinger, 1981). Cobalt oxide was administered to guinea pigs by gavage and 11.3% of the dose was identified in the body (Stokinger, 1981). Elinder and Friberg (1986) reported that gastrointestinal absorption of cobalt ranges from 5 to 45%. Naylor and Harrison (1995) found that gastrointestinal absorption of radiolabeled cobalt citrate decreased markedly with age in rats and guinea pigs. For the current assessment the absorption of ingested cobalt was assumed to range from 18 to 97%.

4.3.1.2 Fraction Absorbed Via Inhalation

After 24 hours, 84% of inhaled cobalt oxide was found to be distributed throughout the body of guinea pigs (Stokinger, 1981). As no additional details were available regarding this study, the inhalation absorption fraction of cobalt was estimated using particle dispersion modelling. The amount of inhaled cobalt which deposits in humans can vary from 50%, for particles with a mean geometric diameter of 0.8 µm, to 75% for particles with a mean diameter of 1.7 µm (Foster *et al.*, 1989). Based on airborne particle dynamics in the respiratory system, approximately 13% of airborne cobalt bound to particulates would be retained in the respiratory system. Assuming 100% bioavailability for this retained fraction, it is expected that 13% of the inhaled cobalt would be absorbed directly from the respiratory system. Additionally, approximately 60% of airborne particles would be cleared by the mucociliary apparatus and swallowed. Assuming that 18 to 97% of the swallowed cobalt is absorbed from the gastrointestinal tract, then 10.8 to 58.2% (18 and 97% of 60%) would be bioavailable by this route. Therefore, based on airborne particle dynamics, the total bioavailability of cobalt from inhaled particles would be 24 to 71% (13%+11%; and 13%+58%).

4.3.1.3 Fraction Absorbed Via Dermal Exposure

Radiolabelled cobalt has been reported to be absorbed through intact human skin (Carson *et al.*, 1987). However, no quantitative estimates for the dermal absorption of cobalt were identified in the literature reviewed for the current assessment. Lacy *et al.* (1996) found that the dermal administration of cobalt resulted in a significantly reduced urinary elimination rate compared to cobalt administered via intramuscular injection. Due to the lack of data, cobalt was assumed to behave in a similar manner to lead; thus the dermal absorption factor for lead

(0.06%) was applied to cobalt. This value of 0.06% is based on inorganic cobalt, as cobalt at the site will not be in the form of soluble salts or as the free ion but will be intrinsically bound within a soil-like matrix from which absorption would be minimal.

4.3.2 Health Hazard Assessment

4.3.2.1 Animal Studies

Acute oral studies with rats have reported LD_{50} values for cobaltous chloride ($CoCl_2$) to range from 150 to 500 mg/kg body weight/day (Elinder and Friberg, 1986).

Various subchronic and chronic studies have been conducted using cobalt mixtures under a variety of exposure conditions. No adverse effects were observed in sheep administered cobalt orally for 109 days (Corrier *et al.*, 1986). Signs of pulmonary disease were observed in miniature swine following inhalation of a cobalt metal powder mixture (50% α and 50% β) at air concentrations of 0.1 and 1.0 mg/m^3 for 6 hours/day, 5 days/week for 3 months (Kerfoot *et al.*, 1975). Animals exhibited a significant decrease in lung compliance and an increase in the amount of collagen in the central areas of the pulmonary alveolar septa. These effects occurred in a concentration-related manner with the compliance values reported as 35.5, 23.3 and 19.8 cm^3/cm H_2O for the control, low and high concentrations, respectively.

Female Sprague-Dawley rats exposed to cobalt metal powder (99.87% pure; median particle size 4 µm) by intratracheal instillation at doses of 0.006, 0.03 and 0.06 mg/kg body weight/day for a period of 4 months displayed no mortality and no outward signs of toxicity (Lasfargues *et al.*, 1995). Animals were dosed once monthly over the duration of the study.

In another inhalation study, adverse effects were observed in F344/N rats and $B6C3F_1$ mice (10/sex/dose) exposed to cobalt sulphate aerosol at air concentrations of 0, 0.3, 1.0, 3.0, 10.0, or 30.0 mg/m^3 for 6 hours/day, 5 days/week, for 13 weeks (Bucher *et al.*, 1990; NTP, 1991). No mortality was observed in treated rats; however, degenerative, inflammatory, and regenerative changes were observed in the respiratory systems of treated animals, including squamous metaplasia in the larynx of rats exposed to the lowest concentration. Increased absolute and relative lung weights were observed in rats exposed to concentrations of 1.0 mg/m^3 or greater. The highest dose group showed decreased body weight, ruffled fur and a hunched posture. In rats exposed to concentrations of 3 mg/m^3 or greater, haematological changes and inflammatory polyps were evident. Mice exposed to the highest cobalt sulphate concentration displayed mortality (2/10 males died), decreased body weight, reduced sperm motility and epididymal weights, an increased number of abnormal sperm and a prolonged estrous cycle. Respiratory system changes, observed primarily in the 2 highest dose groups, included degeneration of olfactory epithelium, squamous metaplasia of respiratory epithelium, and the presence of acute inflammatory exudate in the nasal cavity. Squamous metaplasia was also observed in the larynx of mice exposed to the lowest concentration; similar to what was observed for rats. Since adverse effects were reported in all treated groups, a LOAEL of 0.3 mg/m^3 (the lowest concentration tested) was identified, based on the observed metaplasia of the larynx of both rats and mice. This concentration was corrected for

percent cobalt composition of the compound (*i.e.*, 38.0%) and amortized for duration of exposure. Using the body weight reported in the study for male rats of 0.330 kg and an inhalation rate of 0.322 m^3/day (calculated), the LOAEL of 0.3 mg/m^3 was converted to a dose of 0.02 mg/kg body weight/day [0.3 mg/m^3 x 38.0% x (6/24) x (5/7) x 0.322 m^3/day ÷ 0.330 kg].

A series of studies investigating the lung response of rabbits to a number of cobalt compounds was undertaken by Johansson *et al.* (1983, 1986, 1987). Rabbits exposed to 0.4 and 2.0 mg/m^3 soluble $CoCl_2$ for 1 and 4 months showed an increased number of alveolar macrophages and increased macrophage activity. Rabbits exposed to 0.4 and 2.0 mg/m^3, 6 hours/day, 5 days/week for 14 to 16 weeks displayed nodular aggregation of type II cells, abnormal accumulation of enlarged, vacuolated macrophages, and interstitial inflammation.

Reproductive and Developmental Toxicity Studies

In a study by Domingo *et al.* (1985), female Wistar rats were orally administered $CoCl_2$ during gestation and lactation. Observed effects in the offspring included impaired post-natal development, reduced litter sizes and pup body weights, and decreased liver and spleen weights. No developmental toxicity or teratogenicity was observed in the offspring of Sprague-Dawley rats administered $CoCl_2$ by gavage during gestation (Paternain *et al.*, 1988). However, maternal toxicity was observed at all doses and non-consistent changes in maternal haematology and serum biochemistry were reported. Male rats and mice exhibited no adverse effects on testicular histology and morphology, or on spermatogenic development following intratesticular or subcutaneous injections of cobalt nitrate (Kamboj and Kar, 1964). Conversely, cobaltous chloride administered in drinking water to male mice caused both acute and chronic reproductive effects (Pedigo *et al.*, 1988). Significant decreases in fertility and sperm motility were observed during the first week of the study. Following chronic exposure, decreases in testicular weight, epididymal sperm concentration, fertility and sperm motility were reported. In addition, serum testosterone levels were dramatically increased. Details regarding dose-specific effects were not reported in the study, therefore, this study could not be used to derive an exposure limit. In another study, the fertility of male mice, as indicated by decreased sperm concentration and mobility, was also adversely affected following the administration of cobaltous chloride hexahydrate in drinking water (Pedigo and Vernon, 1993). This same study also found that, following mating with untreated females, significant changes in the percentage of pregnant females, the number of live births and number of preimplantation losses per female occurred.

Mutagenicity, Genotoxicity, and Carcinogenicity Studies

The results of *in vitro* mutagenicity studies suggest that cobalt (II) is non-mutagenic in bacterial systems, as results are predominantly negative (Nishioka, 1975; Kada and Kanemtsu, 1978; Tso and Fung, 1981; Mochizuki and Kada, 1982; Rossman *et al.*, 1984; Ogawa *et al.*, 1986; Wong, 1988). Results in mammalian test systems are mixed as cobalt (II) has produced positive results for induction of DNA damage, mutation, and SCE (Casto *et al.*, 1979; McLean *et al.*, 1982; Andersen, 1983; Hamilton-Koch *et al.*, 1986; Wedrychowski

et al., 1986; Capomazza and Botta, 1991; Hartwig *et al.*, 1991), although negative results for these assays have also been reported (Paton and Allison, 1972; Voroshilin *et al.*, 1978; Amacher and Paillet, 1980; Robinson *et al.*, 1982). Recent studies have suggested that the mutagenic and genotoxic effects of cobalt compounds may be brought about by cobalt-induced generation of free radicals which cause oxidative damage (Hanna *et al.*, 1991). The mutagenicity of cobalt-induced oxidative stress was recently examined in transgenic gpt^+ Chinese hamster cell lines G12 and G10 (Kitahara *et al.*, 1996). Cobalt chloride was found to elicit mutagenic activity 7.7 times greater than the spontaneous mutant frequency in G12 cells, but was only 1.5 to 2.5-fold higher than the spontaneous mutant frequency in G10 cells. The mutation frequency of cobalt sulfide was found to be lower than that for cobalt chloride (Kitahara *et al.*, 1996). In human cell lines, cobalt compounds have tested negative for chromosomal aberrations but have been found to induce micronuclei and DNA strand breaks in human lymphocyte assays (Beyersmann and Hartwig, 1992; Capomazza and Botta, 1991; Van Goethem *et al.*, 1997). Positive results for mutagenicity were also reported in the *Drosophila* wing spot test using $CoCl_2$ (Ogawa *et al.*, 1994). Recently, cobalt (II) ions have been shown to inhibit DNA repair mechanisms in mammalian and bacterial cell lines (Hartwig *et al.*, 1991; Beyersmann, 1994).

In vivo test results have indicated genotoxic potential for cobalt compounds. Cobalt (II) has been reported to cause aneuploidy in the bone marrow and testis of male Syrian hamsters injected intraperitoneally (Farah, 1983). Palit *et al.* (1991) reported that $CoCl_2$ induced chromosomal aberrations in mice following oral administration. Thus, for the current assessment, cobalt (II) was considered to be genotoxic. Studies conducted to assess the genotoxicity of metallic cobalt were not identified in the literature reviewed for the current assessment.

Wehner *et al.* (1977) exposed hamsters to 10 µg cobalt oxide (CoO) per litre of air for 7 hours/day, 5 days/weeks for the animal's lifetime. No increased incidence of tumours was observed. However, pulmonary changes such as interstitial fibrosis, granulomas, hyperplasia of alveolar cells, and emphysema were observed.

In another carcinogenicity study, intratracheal instillation of CoO failed to increase tumour incidence in Sprague-Dawley rats, although an increased incidence of bronchoalveolar proliferation was reported in treated animals (Steinhoff and Mohr, 1991). In a second experiment, the authors reported a higher incidence of squamous cell carcinomas in the lungs of female rats treated with CoO and then benzo[a]pyrene (B[a]P, a known carcinogen), *versus* rats treated with B[a]P only. Stoner *et al.* (1976) reported that subchronic intraperitoneal injection of cobalt (III) acetate in saline failed to increase the incidence of lung tumours in mice. In several other studies (Heath, 1954, 1956; Gilman and Ruckerbauer, 1962; Shabaan *et al.*, 1977; Domingo, 1989; Steinhoff and Mohr, 1991) an increased incidence of localized tumours following subcutaneous/intramuscular injection or implantation has been reported; however, the significance of tumours occurring at injection sites and their relevance to the assessment of human health risks is considered to be questionable (Tomatis, 1977).

The International Agency for Research on Cancer (IARC, 1991) considers the available evidence sufficient to conclude that cobalt metal powder and cobalt (II) oxide are carcinogenic in experimental animals. Evidence for other cobalt compounds is inadequate to classify them as animal carcinogens (IARC, 1991). The American Conference of Governmental Industrial Hygienists (ACGIH, 1996) classified cobalt as Group A3 (animal carcinogen). This classification is applied to agents that are "carcinogenic in experimental animals at a relatively high dose, by route(s) of administration, at site(s), of histologic type(s), or by mechanisms(s) that are not considered relevant to worker exposure."

4.3.2.2 Human Studies

Cobalt is an essential micronutrient in humans, as it is a required element in hydroxycobalamin (vitamin B12). Cobalt is also associated with the regulation of several cofactors and enzymes, and is involved in the production of erythropoeitin (Lison, 1996).

Inorganic cobalt (frequently in the form of cobalt chloride, $CoCl_2$) has been used clinically to induce polycythemia (red blood cell production) for the treatment of anemia associated with a disease state, pregnancy, and to offset blood loss incurred during haemodialysis.

Side effects of the treatment of anemia with cobalt chloride have been reported to be, in general, of little long term or toxicological significance. Immediate effects, including nausea and vomiting, have been reported in some haemodialysis patients at doses of 50 mg $CoCl_2$/d over a 2 to 3-month period (in aqueous solution, a bioavailability-adjusted dose of 0.041 mg Co/kg body weight/day, and in an enteric coated pill, approximately 0.03 mg Co/kg body weight/day) (Bowie and Hurley, 1975; Curtis *et al.*, 1976). Bowie and Hurley (1975) also reported transitory loss of hearing in 3 of 14 patients at 0.041 mg Co/kg body weight/day; assessment of thyroid and liver function indicated no abnormalities in any of the patients. Side effects in anemia patients have been reported to be minimal at 300 mg $CoCl_2$/d for 14 days (Berk *et al.*, 1949), to include nausea and vomiting at 100 mg $CoCl_2$/d (duration of dosing unknown) (Gardner, 1953; Geill, 1969), to include transient tinnitus and nerve deafness at 80 mg/d for 12 weeks or 150 mg $CoCl_2$/d for 4 to 16 weeks (Gardner, 1953), and hypothyroidism in children at 80 to 100 mg $CoCl_2$/d for 3 months (Kriss *et al.*, 1955). Polycythemia without biologically significant side effects was observed in anemic patients at 0.16 to 0.5 mg Co/kg body weight/day for up to 32 weeks (Davis and Fields, 1958; Duckham and Lee, 1976; Taylor *et al.*, 1977). Doses of 0.5 to 0.6 mg Co/kg body weight/day were associated with symptoms of gastric intolerance (Holly, 1955). Administration of 0.5 mg Co/kg body weight/day (32 weeks) and 1.0 mg Co/kg body weight/day (25 days) were not associated with symptoms of cardiomyopathy (Holly, 1955; Davis and Fields, 1958; Duckham and Lee, 1976; Taylor *et al.*, 1977).

Browning (1969) reported that intravenous administration of 5 to 10 mg Co/d to humans (0.1 to 0.5 mg Co/kg body weight/day) (duration of dosing not stated) could cause increased blood pressure, slow respiration, giddiness, palpitation, tinnitus, and nerve deafness.

While the data above indicate that cobalt is generally well tolerated by humans at internal doses (*i.e.*, oral doses corrected for bioavailability) of 0.03 to 0.18 mg Co/kg body weight/day for a subchronic period of time (25 days to 32 weeks), certain individuals less capable of elimination of this element may be at risk of more serious adverse health effects. Curtis *et al.* (1976) reported that of their study group of 23 individuals receiving about 0.03 mg Co/kg body weight/day for 2 to 3 months, 1 person later died of cardiac arrest; it was considered possible that this death was related to cobalt-induced cardiomyopathy. Tissue analyses indicated much higher tissue concentrations of cobalt in this person, in comparison to the other patients. This abnormally high retention was associated with the renal disease, and the authors noted that patients with renal dysfunction tended to have a prolonged retention of cobalt in comparison to persons with normal renal function. This was postulated to predispose the renally-impaired patients to possible adverse effects of cobalt treatment. Bowie and Hurley (1975) also noted variation in cobalt tissue concentrations amongst haemodialysis patients.

It has been postulated that cobalt may be capable of inducing dermatitis in previously sensitized individuals (*e.g.*, eczema sufferers) (U.S. EPA, 1997).

Another source of data on the potential toxic effects of cobalt on humans has been the "beer-cobalt" incidents observed in certain populations of Canada, the United States, and Belgium. Cobalt was added to beer as a foam stabilizer, and it was discovered that 43% of a population of people ingesting large quantities of this beer (8 to 30 pints per day, associated with cobalt ingestion of 0.04 to 0.14 mg/kg body weight/day) later developed cardiomyopathy characterized by mild congestive heart failure, low cardiac output, metabolic acidosis and in some instances with heavy drinkers, death due to both acute and delayed effects (*e.g.*, Alexander, 1969, 1972; Morin *et al.*, 1971). U.S. EPA (1997) noted that the cardiomyopathy may have been due to pre-existing cardiac and hepatic conditions due to alcohol abuse, and to protein-poor nutritional habits. In the light of the data obtained with anaemic patients administered oral doses of up to 1 mg/kg body weight/day without cardiomyopathy, this analysis seems probable. Indeed, a laboratory study by Rona (1971) in rats indicated that a diet poor in proteins, but high in cobalt, resulted in signs of cardiomyopathy. Seghezzi *et al.* (1994) also concluded that an interaction between poor nutrition, alcohol abuse and cobalt exposure may have been responsible for the observed cardiomyopathies.

The majority of the available studies investigating human exposure to cobalt have been in occupational settings where inhalation of dusts and particles is the primary exposure route, with dermal exposure generally occurring to a lesser extent.

Acute effects of exposure to cobalt-containing dust are typically inflammation of the nasopharynx; however it is unclear if this results from a non-specific irritant effect or from an immunologically-mediated reaction (*e.g.*, allergic rhinitis) (Lison, 1996). Contact dermatitis has also been consistently reported upon acute dermal exposure to cobalt compounds (Fischer and Rystedt, 1983).

Numerous studies have associated longterm occupational exposure to a variety of cobalt compounds with bronchial asthma in a small proportion of workers (Bruckner, 1967; Cugell *et al.*, 1990; Roto, 1980; Raffin *et al.*, 1988; Davison *et al.*, 1983; Kusaka *et al.*, 1986; Shirakawa *et al.*, 1989; Gheysens *et al.*, 1985; VanCutsem *et al.*, 1987). The risk of asthma has been estimated to increase by as much as 5-fold when cobalt air concentrations are greater than or equal to 100 $\mu g/m^3$ (Roto, 1980). There is strong evidence to suggest that cobalt is a causative agent for occupational asthma, although the mechanism of action has not yet been determined (Cugell, 1998). A number of studies have indicated that the cause of cobalt-induced asthma may be an allergic reaction to cobalt-containing dusts (Kusaka *et al.*, 1989, 1990; Shirakawa *et al.*, 1988). The causative role of cobalt in asthma is supported by evidence of affected workers showing partial or complete remission of asthma when removed from the source of exposure, after wearing respirators or after the installation of exhaust ventilation systems (Kusaka *et al.*, 1990). Chronic exposure to cobalt dusts may also lead to the development of a moderate obstructive syndrome, possibly the result of non-specific irritation (Kusaka *et al.*, 1986).

The effects of cobalt exposure in humans have been reported in several studies conducted with workers in the cemented carbide industry, which uses cobalt in its processes. Respiratory disease with symptoms ranging from shortness of breath and coughing to permanent disability or death in a very few cases has been reported in some workers (Miller *et al.*, 1953; Lundgren and Ohman, 1954). In addition, interstitial lung disease (hard-metal disease) and "airways disease" have been reported in tungsten carbide workers (Sjogren *et al.*, 1980), and in a male worker polishing disks containing cobalt (Nemery *et al.*, 1990).

Preliminary results from a study investigating the effects of cobalt-containing dust on lung function indicated that prolonged exposure (>5 years) led to spirometric disturbances compatible with a moderate restrictive syndrome (Gennart and Lauwerys, 1990). Airborne concentrations of cobalt frequently exceeded the current ACGIH threshold limit value (TLV) of 50 $\mu g/m^3$ in the workplace environment studied. Sprince *et al.* (1988) conducted a cross-sectional morbidity study of workers in the tungsten carbide industry and reported a low incidence of abnormal chest radiographs and an absence of impact on lung function. However, using a logistic regression model the authors reported that the relative odds of developing a work-related respiratory wheeze doubled when the exposure exceeded 50 $\mu g/m^3$, as compared to exposures below 50 $\mu g/m^3$.

Raffin *et al.* (1988) reported that cobalt may have been a causative agent in the development of impaired lung function in cobalt-exposed Danish pottery painters. Other adverse effects which have been associated with occupational exposure to cobalt include fibrosis, pneumoconiosis, coughing, conjunctivitis, rhinitis, pharyngitis, dyspnea, alveolitis, pneumonia, allergic dermatitis, cardiomyopathy, ischemic heart disease, polycythemia, progressive hearing loss, atrophy of the optic nerve, and altered thyroid hormone metabolism (Cugell, 1998; Meecham and Humphreys, 1991; Barborik and Dusek, 1972; Kennedy *et al.*, 1981; Lison, 1996; Prescott *et al.*, 1992). Franchini *et al.* (1994) found no association between cobalt exposure and kidney dysfunction in hard metal tool workers.

A recent retrospective cohort study investigated the incidence of lung cancer associated with exposure to cobalt (Tüchsen *et al.*, 1996). A cohort of 872 women occupationally exposed to cobalt-aluminate spinel in 2 Danish porcelain factories was compared to a reference cohort of 520 women not exposed to cobalt, who also worked in these 2 factories over a 5-year period. No significant differences in cancer mortality were observed. A slight increase in lung cancer incidence was found in both the exposed and reference group, compared to the background incidence rate for all Danish women. The exposed group had only a slightly higher lung cancer incidence than the reference group (RR ratio for exposed group : reference group = 1.2). Measured cobalt air concentrations ranged from non-detectable to approximately 200 $\mu g/m^3$, with one extremely high concentration (861 $\mu g/m^3$) reported in one year. The authors acknowledged that the study was based on a small number of subjects and recommended a follow-up study once data for another 5-year period was available.

There are a number of factors which preclude the use of the above human occupational and/or epidemiological data in deriving a human exposure limit. The age, lifestyle and health status of the workers, as well as the duration and characterization of exposure, were not adequately quantified in any of these studies. In addition, many of these studies had flawed experimental designs such as lack of a control or reference group, and not accounting for concurrent exposures to other agents (chemical and biological). Furthermore, air concentrations of cobalt were either not reported or were reported in an inconsistent manner, such that effects could not be attributed to measured exposure concentrations.

In a review of the carcinogenicity of cobalt metal and other cobalt compounds, Leonard and Lauwerys (1990) concluded that there was insufficient evidence to implicate cobalt or cobalt compounds as human carcinogens. Cobalt and its compounds presently have an IARC classification of 2B; possibly carcinogenic to humans (IARC, 1991).

4.3.3 Exposure Limits

A tentative TLV for cobalt was set at 0.1 mg/m^3 in 1966, as this concentration of cobalt metal fumes and/or dusts could be achieved without economic or technical difficulty, and appeared to protect against hypersensitivity reactions (ACGIH, 1991). However, based on the results of a study by Kerfoot *et al.* (1975) which demonstrated adverse pulmonary effects at the TLV of 0.1 mg/m^3 in miniature swine, a recommendation was made to lower the TLV to a time weighted average (TWA) of 0.05 mg/m^3 (0.007 mg/kg body weight, assuming an average breathing rate of 10 m^3/8 hours and a body weight of 70 kg) (ACGIH, 1991). However, in 1994 a lower TLV of 0.02 mg/m^3 was established for elemental and inorganic cobalt (ACGIH, 1996). The Ontario Ministry of the Environment (OMOE, 1994) proposes a 24-h reference concentration (RfC) of 0.1 $\mu g/m^3$ for cobalt and its compounds.

Cobalt has been classified by the ACGIH as an A3 carcinogen. This classification applies to animal carcinogens that are "not likely to cause cancer in humans except under uncommon or unlikely routes or levels of exposure" (ACGIH, 1996). The International Agency for Research on Cancer (IARC, 1991) considers the available evidence on carcinogenicity inadequate for cobalt compounds in humans and has designated cobalt and its compounds as

2B; possible human carcinogens. For the current assessment, cobalt was not considered to be a human carcinogen, therefore regulatory RfD's were used as the exposure limits.

The U.S. EPA Region III derived an oral RfD of 60 µg/kg body weight/day for cobalt based on cobalt intake levels in food (U.S. EPA, 1997). This RfD was based on the upper range of average intake for children (60 µg/kg/day), that is below the levels of cobalt needed to induce polycythemia in both renally compromised patients (180 µg/kg body weight/day) and normal patients (960 µg/kg body weight/day). However, the current U.S. EPA IRIS list of chemicals does not include cobalt (U.S. EPA, 1998).

An inhalation RfD of 0.01 µg/kg body weight/day is proposed by the Agency for Toxic Substances and Disease Registry (ATSDR, 1997) of the U.S. Public Health Service. This inhalation RfD was derived by ATSDR based on the NTP (1991) and Bucher *et al.* (1990) studies, where a LOAEL of 0.3 mg/m^3 was identified, based on metaplasia of the larynx in rats and mice.

No regulatory dermal exposure limits were identified in the literature reviewed for the current assessment.

For the purposes of this assessment, the human bioavailability of cobalt was assumed to be 18 to 97% for ingestion, 24 to 71% for inhalation and 0.06% for dermal exposures.

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CANTOX ENVIRONMENTAL

PART 4.4
TOXICOLOGICAL REVIEW: LEAD

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4.4.0 TOXICOLOGICAL REVIEW: LEAD

4.4.1 Fraction Absorbed *Via* Different Routes

4.4.1.1 Fraction Absorbed Via Ingestion

In clinical studies, adults have been found to absorb approximately 10 to 15% of their total oral lead intake (Kehoe, 1961; Thompson, 1971; Karhausen, 1973; Blake, 1976; Chamberlain *et al.* 1978). Estimated absorption values are dependent on both the chemical and physical forms of ingested lead (Barltrop and Meek, 1975), as well as age and diet. In a recent review, Mushak (1991) reported that small children and infants absorb as much as 42 to 53% of their lead intake (Karhausen, 1973; Alexander, 1974; Ziegler *et al.*, 1978). Dietary deficiencies of iron, Vitamin C or D, and low dietary intake of fibre and milk can significantly increase gastrointestinal lead absorption for young children and nursing infants (Garber and Wei, 1974; Stephens and Waldron, 1975; Sorrell *et al.*, 1977; HWC, 1980). For the current assessment, the oral bioavailability of lead was assumed to be 10 to 15% for adults and 42 to 53% for children and infants.

4.4.1.2 Fraction Absorbed Via Inhalation

The World Health Organization (WHO, 1984) estimated that approximately 20 to 60% of the total amount of lead inhaled is deposited in the lung, with the majority of this being absorbed. Kehoe (1961) and Gross (1981) obtained human respiratory system lead deposition rates of 30 to 70% (mean of 48%) while Nozaki (1966), Chamberlain *et al.* (1975), Morrow *et al.* (1980), and Hammond *et al.* (1981) cited similar values of 30 to 50%. Lead deposition rates can vary depending on the respiration rates of the subjects used in the studies, and the actual particle size. It is estimated that most of the lead deposited in the pulmonary region is either absorbed or cleared, since autopsies on human lungs have shown that very little lead is accumulated in the lung (Barry, 1975). Specific absorption values of lead from the respiratory system of children were not available, but Barltrop (1972) estimated that children inhale 40% more lead than adults. The lead deposition rate in 10-year old children was estimated by James (1978) to be 1.6 to 2.7 times that of adults, based on a number of modifying factors, including differences in metabolic rates and airway dimensions. The percentage of inhaled lead that is swallowed following clearance from the respiratory system (from the action of the mucociliary apparatus) was reported to be 6% (Chamberlain *et al.* 1975).

For the current assessment, lead was assumed to be adsorbed to airborne particles or to soil particles which have become suspended in the air. Therefore, the bioavailability of lead following inhalation would be determined by the dynamics of deposition, retention and clearance of airborne particles by the respiratory system. Based on the airborne particle dynamics model, 13% of lead adsorbed to airborne particles would be retained in the respiratory system, while 60% of airborne particles would be cleared from the respiratory system and swallowed. In adults, it was assumed that 10 to 15% of the lead adsorbed to

swallowed particulates would be absorbed from the gastrointestinal tract, thus 6 to 9% of airborne lead would be bioavailable by this route (*i.e.*, 10% of 60%; 15% of 60%). Assuming 100% bioavailability for the retained fraction of lead, 13% of inhaled lead would be absorbed by the respiratory system. Therefore, for adults, the total fraction of airborne lead that would be bioavailable following inhalation would be 19 to 22% (13% from the respiratory tract plus 6 to 9% from the gut). For children, it was assumed that 42 to 53% of the lead adsorbed to swallowed particles would be absorbed, thus an additional 25.2 to 31.8% of airborne lead would be bioavailable by this route (42% of 60%; 53 % of 60%). Therefore, for children the total fraction of airborne lead that would be bioavailable following inhalation would be 38.2 to 44.8% (13% from the respiratory tract plus 25.2 to 31.8% from the gut).

4.4.1.3 Fraction Absorbed Via Dermal Exposure

The absorption of inorganic lead compounds through the skin is generally considered negligible compared to the proportion absorbed from either inhalation or ingestion. Skin absorption of lead acetate was estimated to approach 0.06% while up to 8% absorption was reported for the organo-lead compound, tetraethyl lead (Moore *et al.*, 1980). A series of studies conducted with human volunteers had shown that lead salts, such as lead chloride and lead nitrate, are rapidly absorbed through the skin when applied in aqueous solution, resulting in elevated lead concentrations in sweat and saliva, but not blood (Lilley *et al.*, 1988; Florence *et al.*, 1988; Stauber *et al.*, 1994). However, these studies were not able to accurately quantify the amount of lead absorbed or determine which tissues, if any accumulated lead through this route (Florence *et al.*, 1998). A recent study in which aqueous solutions of lead acetate or nitrate were applied to the skin of mice, found that 0.04% of the administered dose was absorbed through the skin in less than 24 hours (Florence *et al.*, 1998). Elevated lead concentrations were detected in mouse skin, muscle, pancreas, spleen, kidney, liver, caecum, bone, heart and brain but not in the blood. The authors concluded that blood lead, the prime index of lead status in human populations, is not indicative of dermal exposure; thus the dermal route may require special consideration when assessing population exposure to lead.

For the current assessment, the dermal bioavailability of lead was assumed to be 0.06%. This estimate is considered appropriate as the lead at the site would not be present in the form of soluble salts, the free ion, or as an organo-lead compound, but would be intrinsically bound within a soil-like matrix; thus the amount of lead available for absorption *via* this route would be minimal.

4.4.2 Health Hazard Assessment

4.4.2.1 Genotoxicity and Mutagenicity Studies

In an *in vivo* study in which mice were administered 0, 0.625, 1.25, 2.5, 5, 10, 20, 40, and 80 mg/kg body weight of lead nitrate in drinking water or intraperitoneally, a significant increase in the frequency of micronuclei in mouse bone marrow cells was observed at 12, 24, and 36

hours post-treatment (Jagetia and Aruna, 1998). However, the increased frequency of micronuclei fluctuated and was not dose-related. Male mice were found to be more sensitive to the induction of micronuclei than female mice. The increased frequency of micronuclei may be due to DNA strand breaks by lead nitrate, as this compound has been found to induce DNA strand breaks in fresh water mussel foot cells (Black *et al.*, 1996).

The results of other *in vivo* studies have indicated an increase in chromosomal deletion in fetal liver and maternal bone marrow of pregnant mice treated with lead nitrate (Nayak *et al.*, 1989a,b). In general, studies on the clastogenic effects of lead are contradictory. Increased frequencies of chromosomal aberrations and sister chromatid exchange (SCE) have been reported in human lymphocytes after treatment with lead acetate and lead sulphate (Beek and Obe, 1974; Obe *et al.*, 1975; Wulf, 1980). Increased SCE frequencies were also observed in Chinese hamster ovary (CHO) cells after lead nitrate treatment; however, micronuclei frequency was not affected (Lin *et al.*, 1994). Lead has also been reported to activate DNA synthesis *in vitro* (Sirover and Loeb, 1976), and inhibit nucleic acid and protein synthesis (Skreb and Habazain-Novak, 1975). In contrast, no significant increase in the frequency of chromosomal aberration and micronuclei in cultured peripheral blood lymphocytes was reported following lead exposure (Schmid *et al.*, 1972; Hoffman *et al.*,1984). Also, CHO cells exposed to lead acetate did not show significant changes in the frequency of chromosomal aberrations (Bauchinger and Schmid, 1972).

4.4.2.2 Animal Studies

Acute Toxicity Studies

In an *in vitro* study, glial blastoma cells incubated with 1 µM lead for 3 to 4 days showed impairment of glial cell differentiation and induction of undifferentiated cell growth (Stark *et al.*, 1992). This may lead to neurotoxic effects during embryonic development if lead is able to access developing glial cells by passing through the blood-brain barrier.

Various biochemical effects have been associated with lead exposure and elevated blood lead (PbB) concentrations. The cytoplasmic enzymes, delta-amino-levulinic acid dehydratase (ALAD) and haem synthetase are inhibited by lead and result in the increase of their respective substrates delta-amino-levulinic acid (ALA) in serum and urine, and "free" erythrocyte protoporphyrin (FEP) in blood (Nutrition Foundation, 1982; Zareba and Chmielnicka, 1992). An increase in urine coproporphyria has also been associated with elevated PbB (Zareba and Chmielnicka, 1992). The presence of lead in blood reduces the bioavailability of iron for haem synthesis. In response to reduced haem formation, concentrations of the rate-limiting enzyme, delta-amino-levulinic acid synthetase (ALAS) is increased, and hemoglobin biosynthesis is decreased, eventually leading to reduced numbers of red blood cells. Other responses include erythroid hyperplasia, reticulocytosis and microcytosis. ALAD is present in excessive amounts and is not the rate-limiting enzyme in the biochemical pathway of haem synthesis. As a result, partial inhibition of ALAD is not considered to be toxicologically significant (Nutrition Foundation, 1982).

Chandravathy *et al.* (1997) found that healthy male Swiss albino mice orally exposed to 33 mg/kg body weight lead nitrate for 21 days displayed a range of hematological responses. These effects included significant reductions in red blood cell counts, hemoglobin concentrations, packed cell volume, as well as a slight decrease in differential leukocyte count, and an increase in mean corpuscular volume, and mean corpuscular hemoglobin.

Recently, it was found that acute exposure to lead potentiates some estrogenic responses and inhibits others; thus lead may act as a weak estrogen or antiestrogen (Tchernitchin *et al.*, 1998). Female Sprague-Dawley rats intravenously administered 75 mg/kg body weight lead acetate 1 or 24 hours before hormone treatment showed signs of estrogenic stimulation in the uterus for a number of parameters, while others were inhibited or had no change.

Subchronic and Chronic Toxicity Studies

Subchronic and chronic exposure of rodents to lead has resulted in intranuclear inclusion bodies in the proximal tubular epithelium of the kidney, as well as functional and ultrastructural changes in the kidney mitochondria leading to hyperaminoaciduria, glycosuria and hyperphosphaturia, at concentrations of lead in the blood of >70 µg/dL (Nutrition Foundation, 1982). Cooke *et al* (1990) reported that administration of 200 mg lead/L as $Pb(NO_3)$ to wood mice in drinking water for 30 days resulted in significantly elevated concentrations of lead in the femur tissue and kidneys; the later is associated with inclusion bodies accompanied by degeneration of tissue. Accumulations of lead in the bone tissue may adversely affect the ability of bone to accumulate fluoride (Cerlewski and Ridlington, 1987). Lead accumulation in bone tissue may also inhibit axial bone development and reduce bone mass and density (Escribano *et al.*, 1997). Newborn male Sprague-Dawley rats treated intraperitoneally with lead acetate showed delayed eye opening and decreased balance (Luthman *et al.*, 1992). In another study, male Sprague-Dawley rats dosed with lead showed decreased body weight gains, increased incidence of spinal cord lesions, and increased concentrations of lead in brain tissue (Yagminas *et al.*, 1992).

Substantial species differences in susceptibility to the behavioural effects of lead have been clearly demonstrated in laboratory animals, with monkeys being one of the most sensitive species (Nutrition Foundation, 1982). Rats developed signs of hyperactivity at blood lead concentrations (PbB) of 40 to 60 µg/dL (Overmann, 1977) with transient hyperactivity observed at PbB concentrations of 20 to 59 µg/dL. Similarly, Golter and Michaelson (1975) reported increased activity in rats orally administered 1.09 mg lead/day as lead acetate solution. Monkeys demonstrated enhanced agitation at blood lead concentrations (PbB) ranging from 33.1 to 42.9 µg/dL (Levin *et al.*, 1988). When PbB concentrations were 11 to 13 µg/dL, 3-year old monkeys, exposed to lead from birth, showed impaired responses in discrimination reversal tasks, non-spatial form discrimination and non-spatial colour discrimination (Rice, 1985). However, the PbB concentrations in these monkeys had been much greater when they were infants fed milk-only diets. Monkeys with average PbB concentrations of 33.1 to 42.9 µg/dL experienced decreased visual attentiveness (Levin *et al.*, 1988). Monkeys showed impaired learning and decreased visual acuity for a variety of tasks

at PbB concentrations ranging from less than 40 to 85 µg/dL (Bushnell *et al.*, 1977; Bushnell and Bowman, 1979; Rice *et al.*, 1979; Rice and Willes, 1979).

Rice (1992a) examined the behavioural effects of lead on newborn monkeys orally dosed with lead acetate to yield a blood concentration plateau of 33 µg/dL. No discrimination reversal impairment, and no differences in behavioural delayed alternation were observed; however, differences in performance were observed in the differential reinforcement of low rate schedule (DRL) behavioural test, and in the monkeys' ability to learn visual discrimination. In further work with monkeys, Rice (1992b) gave oral doses of lead in groups characterized by the following dosing regimes: Group 1, vehicle only (control); Group 2, lead continuously from birth (PbB 32 to 36 µg/dL); Group 3, lead continuously from birth to 400 days followed by vehicle only (PbB 32 to 36 µg/dL); and, Group 4, vehicle only from birth to 300 days of age followed by exposure to lead (PbB 19 to 26 µg/dL). Two different non-spatial discrimination reversal tasks used to determine the behavioural effects of lead on treated monkeys indicated significant impairment in Groups 2 and 4, while Group 3 was marginally impaired.

Reproductive and Developmental Toxicity Studies

The effects of lead on growth in female rats and on growth and skeletal development in their offspring were investigated by Hamilton and O'Flaherty (1994). No alteration in growth rate was observed in weanling females continuously exposed to lead in drinking water and fed a replete diet. After 49 days of exposure, rats were mated with control males. At parturition, 1 group of previously exposed lactating dams were given control drinking water, while other lactating dams from the control group were given lead in drinking water. The authors indicated that lead exposure prior to parturition caused greater maternal tibial lead accumulation than lead exposure after parturition. In contrast, lead exposure prior to parturition had a lesser impact on offspring tibial lead accumulation than lead exposure after parturition. Also, offspring body weight was depressed and continuous lead exposure caused a greater decrease in offspring body weight than lead exposure prior to, or after parturition. Other observed effects in offspring included decreased tail length growth, increased weanling growth-plate width, disruption of chondrocyte organization, and wider metaphyseal trabeculae.

In a study by Hamilton *et al.* (1994), offspring of pregnant female rats exposed to lead in their drinking water during gestation had decreased fetal body weights. Similar results were reported for mice exposed *via* drinking water (Pinon-Lataillade *et al.* 1995). The exposed offspring were then mated with unexposed mates to determine lead exposure on subsequent generations. The authors reported reduced litter sizes for females and reduced body, testes, epididymis, seminal vesicle and ventral prostate weights in males. Junaid *et al.* (1997) exposed mice to lead acetate by oral gavage to examine ovarian follicular development. Results showed that small, medium and large follicles were significantly affected by the lead and atresia also occurred in the medium follicles. A study by Kristensen *et al.* (1995) indicated a synergistic effect causing suppression of the development of primordial oocytes

during fetal life and a longer gestation period in mice exposed to lead and benzo[a]pyrene (BaP) in drinking water. These results were not found in mice exposed to either lead or BaP alone.

In order to assess endocrine effects of lead, Kempinas *et al.* (1994) acutely and chronically exposed pubertal rats to lead acetate *via* drinking water and injection. Following acute exposures, the animals had increased levels of testosterone in both plasma and in testes; however, circulating levels of leuteinizing hormone (LH) were not affected in either group. Another reproductive study by Ronis *et al.* (1996) exposed rats to lead acetate in drinking water during *in utero*, prepubertal or postpubertal development stages. Results reported for males included decreased secondary sex organ weights (prepubertal) and suppressed prepubertal growth and serum testosterone levels (*in utero*). Female rats were reported to have delayed vaginal opening and disrupted estrus cycling (prepubertal), as well as suppressed prepubertal growth and circulating estradiol levels (*in utero*).

A more recent study by Ronis *et al.* (1998a) continuously exposed Sprague-Dawley rats to 0.6%
lead acetate in drinking water (available *ad libitum*) for the following periods: gestational day 5 through birth; during pregnancy and lactation; during lactation only; from birth through adulthood; and from gestational day 5 through adulthood. Relative weights of male secondary sex organs in adult offspring were not significantly affected in any treatment group. Female pups exposed to lead from birth through adulthood or from gestational day 5 through adulthood displayed significantly delayed vaginal opening and disrupted estrus cycling. Significant depression of adult mean serum testosterone levels was observed male pups exposed to lead from gestational day 5 through adulthood. Lead exposure decreased birth weights in all animals exposed *in utero*, and mean body weights were significantly decreased in all treatment groups up to weaning. All treatment groups had significantly reduced growth rates during lactation. Male pups exposed to lead during pregnancy and lactation, from birth or gestational day 5, had significantly reduced growth rates during puberty. Post-pubertal growth rates were unaffected in all treatment groups. In 2 other reproductive and developmental toxicity studies with Sprague-Dawley rats (Ronis *et al.*, 1998b,c), where lead acetate was orally administered (0.05% to 0.45% w/v) beginning on gestational day 5, reductions were observed in birth weights, pre-pubertal and pubertal growth rates, serum IGF_1, plasma sex steroids, and plasma luteinizing hormone (LH). Significant increases in pituitary growth hormone and pituitary LH levels were also observed. The authors suggest that the mechanism of toxicity for the observed reproductive and developmental effects of lead involves disruption of growth hormone and luteinizing hormone secretion during puberty.

Offspring of female Wistar rats orally administered 1.0 mM lead acetate in drinking water displayed a hastened appearance of eye opening, startle reflex and negative geotaxis, while spontaneous alternation performance was hindered relative to controls (Mello *et al.*, 1998). Nagymajtényi *et al.* (1998) treated Wistar rats with 80, 160, and 320 mg/kg body weight lead acetate by gavage during days 5 to 15 of pregnancy, or days 5 to 15 of pregnancy + 4 weeks

of lactation, or days 5 to 15 of pregnancy + 4 weeks of lactation + 8 weeks post-weaning. F1 male rats exposed to lead during pregnancy only displayed an increased hyperactivity and grooming behaviour. Electrophysiological functions in F1 male rats showed dose and treatment-dependent changes as well.

Effects of chronic lead exposure on testis ultrastructure were examined in the cynomolgus monkey after oral administration of lead acetate (1500 µg/kg body weight/day) in the following groups: birth to 10 years (lifetime); postnatal day 300 to 10 years (postinfancy); and postnatal 0 to 400 (infancy) (Foster *et al.*, 1998). At age 10 years, circulating blood lead (PbB) concentrations in the lifetime and postinfancy treatment groups was approximately 35 µg/dL. Sertoli and spermatogenic cells of monkeys from the infancy and lifetime groups revealed injuries, and ultrastructural changes in the testis. Thus, chronic lead exposure resulting in moderate PbB concentrations induced persistent ultrastructural changes in the testis of the cynomolgus monkey.

Exposure to lead during developmental stages may also result in immunotoxicity in the offspring. Nine-week old female Fischer 344 rats were prenatally exposed to lead acetate administered to dams in drinking water at concentrations of 0, 100, 250, and 500 ppm during breeding and pregnancy (Miller *et al.*, 1998). Macrophage cytokine and effector function properties were elevated in the 250 ppm dose group, while cell-mediated immunity was depressed. Interferon levels were decreased in the 500 ppm dose group and serum IgE levels were increased in the 100 ppm group. The authors concluded that maternal exposure to moderate lead concentrations produces chronic immune modulation in F344 rat offspring exposed *in utero*. The dams showed no immune alterations at any of the dose levels tested.

Carcinogenicity Studies

In a chronic study by Azar *et al.* (1973), rats were administered dietary lead acetate in doses of up to 500 ppm for 2 years. In a second 2-year study, rats were fed diets containing lead acetate in doses of 0, 1,000, and 2,000 ppm. No renal tumours were reported in animals receiving 10 to 100 ppm lead acetate; however, males fed 1,000 and 2,000 ppm lead acetate had an increased renal tumour incidence. Despite the evidence of tumours at 1,000 and 2,000 ppm dietary lead acetate however, the U.S. EPA (1998) considered this study to be questionable due to the lack of experimental details that were reported.

In several studies, extreme dietary exposures to lead salts which produced nephrotoxicity have been shown to induce renal neoplasms in rats, mice and hamsters (Boyland *et al.*, 1962; Van Esch *et al.*, 1962; Zawirska and Medras, 1968; Jessup and Shott, 1969; Van Esch and Kroes, 1969; NCI, 1978; Koller *et al.*, 1985). It is doubtful, however, that the extreme exposures and renal tissue concentrations of lead necessary for carcinogenicity in rodents would ever occur in humans because of the degree of toxicity of lead to the central nervous system (CNS) (Nutrition Foundation, 1982). No other target sites for tumour formation from lead exposure have been identified. Therefore, for the current assessment, lead was not considered to be a carcinogen.

4.4.2.3 Human Studies

The threshold PbB concentration for lead-induced increases in free erythrocyte porphyrin (FEP) is in the range of 25 to 30 µg/dL whole blood in women and children (Nutrition Foundation, 1982) and in adult males (Landrigan, 1991). Studies of children living in proximity to a lead smelter indicated an apparent threshold of 60 µg/dL or greater for effects on FEP (McNeil *et al.*, 1975; Landrigan *et al.*, 1976). The apparent discrepancy in the PbB concentration threshold for children resulted from the presence of an iron deficiency in children with the lesser threshold compared with those living near the smelter. PbB concentrations of about 5 µg/dL have been associated with inhibited ALAD activity in children (Chisolm *et al.*, 1985), although this is of doubtful toxicological significance (Nutrition Foundation, 1982).

PbB concentrations are directly related to anaemia (Landrigan, 1991) resulting from impairment of haem synthesis and acceleration of red blood cell destruction. The threshold for this effect in children has been reported to be 50 µg/dL (Tsuchiya, 1979; Nutrition Foundation, 1982). Ferrochelatase, which catalyses the transfer of iron from ferritin into protoporphyrin to form haem is inhibited by lead which results in an increased excretion of coproporphyrin in the urine and accumulation of FEP (Landrigan, 1991). Elevated delta-amino-levulinic acid and coproporphyrins in the urine were reported in children and adults with PbB concentrations in the range of 30 to 40 µg/dL. While elevated PbB concentrations are clearly associated with anemia, the precise mechanism of this effect is unclear. It has been hypothesized that, in addition to impaired haem synthesis and ferrochelatase inhibition, the inhibition of erythropoietin synthesis may be an important factor leading to lead-induced anemia (Factor-Litvak *et al.*, 1998). Erythropoietin is a hormone produced mainly in the proximal renal tubule which regulates both steady-state and accelerated erythrocyte production (Erslev and Caro, 1986). Levels of this hormone have been shown to be significantly depressed in pregnant women with moderately elevated PbB concentrations (Graziano *et al.*, 1991). A prospective study with children aged 4.5, 6.5, and 9.5 years (n=211, 178, and 234, respectively), found a positive association between PbB and erythropoietin concentrations (Factor-Litvak *et al.*, 1998). The association was strongest in children aged 4.5 years and weakened considerably by 9.5 years. Mean PbB concentrations in the 4.5-yeargroup were 38.9 µg/dL, and 28.2 µg/dL in the 9.5-yeargroup. None of the children in the study showed signs of anemia however. It was concluded that in lead-exposed children, normal hemoglobin maintenance requires hyperproduction of erythropoietin. As children age and continue to be exposed to lead, this compensatory mechanism appears to be failing, suggesting a gradual loss of renal endocrine function in association with chronic lead exposure (Factor-Litvak *et al.*, 1998).

In an environmental exposure study (Staessen *et al.*, 1990), London civil servants not exposed to heavy metals on an industrial basis had PbB concentrations which were positively correlated with the number of cigarettes smoked per day, serum gamma-glutamyltranspeptidase, and with serum creatinine concentration in men only (possibly due to lead effects on renal functions). PbB concentration was higher in men and in postmenopausal

women than in premenopausal women which suggests sex differences in lead pharmacokinetics. The authors indicated that there seems to be postmenopausal demineralization of bone, which can increase PbB concentrations by 25%.

In a critical review of the neuropsychological effect of lead in occupationally exposed workers, Ehle and McKee (1990) considered the available data to be inconclusive with respect to psychological and neuropsychological effects from low-level exposure in adults (PbB <60 µg/dL). However, the authors noted that subtle changes or differences in psychomotor and cognitive functions may serve as early warning signals. Workers exposed to lead have exhibited symptoms such as fatigue, irritability, inability to concentrate for prolonged periods of time as well as neurological problems which include disorders in verbal intelligence, memory, and perpetual speed (Baker *et al.*, 1990). PbB concentrations in excess of 100 to 120 µg/dL in adults have been associated with acute lead encephalopathy which can cause effects such as confusion, disorientation, stupor, convulsions, coma and even death (Ehle and McKee, 1990). However, these cases have often resulted from exposure to lead through consumption of contaminated alcohol; thus, symptoms likely reflect both lead and alcohol toxicity. Male workers from a storage battery plant (n=25), with a mean PbB concentration of 74.8 µg/dL showed a significant decrease in chemotaxis and random migration of neutrophils, relative to controls where the mean PbB concentration was 16.7 µg/dL (Undeğer and Basaran, 1998). The results of this study suggest that chronic occupational lead exposure may diminish neutrophil function, which may result in a reduced immunological response to infections. Two male smelter workers with PbB concentrations of 105.6 and 76.5 µg/dL, respectively, showed significantly delayed values for motor and sensory nerve conduction velocities and evoked potentials, relative to controls (Fujimara *et al.*, 1998). A general finding of this study was that peripheral nerves appear to be more sensitive to lead than the CNS, possibly due to the blood-brain barrier or impairment of slow axonal transport in peripheral nerves by lead (Yokoyama and Araki, 1992). The WHO (1995) has suggested that subclinical effects of occupational lead exposure occur at 30 µg/dL for delayed nerve conduction velocities, 35 µg/dL for interval variability changes, and 40 µg/dL for neurobehavioural changes.

In a study by Fischbein (1992), lead concentrations in the air and in the blood of individuals at firing ranges were examined. In 1978, it was reported that 26% of subjects showed CNS symptoms and 16% showed gastrointestinal symptoms. In another study, Lin and Lim (1992) examined the potential association between lead urinary levels and renal diseases in Chinese patients. The authors concluded that the development of renal failure may be a result of exposure to elevated lead concentrations; however, confounding factors could not be ruled out.

Other studies however, clearly show an association between lead exposure and renal diseases. Renal symptoms of acute lead poisoning include glycosuria, aminoaciduria, and phosphaturia, collectively called Fanconi syndrome (Loghman-Adham, 1997; Chisholm *et al.*, 1995). These effects are believed to be the result of lead-induced inhibition of mitochondrial respiration and phosphorylation (Goyer, 1989). A PbB level of 60 µg/dL

appears to be the threshold for proximal tubule injury in both animals and humans (Goyer and Mahaffey, 1972). Symptoms of acute lead poisoning are usually reversible following chelation therapy and cessation of lead exposure (Goyer, 1989). However, chronic lead exposure may result in irreversible kidney-related changes such as interstitial fibrosis, tubular atrophy, and glomerular sclerosis, as well as hypertension and gout (Goyer, 1989; Nolan and Shaikh, 1992; Morgan *et al.,* 1996). Attempts to correlate persistent renal dysfunction with chronic lead exposure during childhood have produced mixed results. Tepper (1963) reported a follow-up study of 165 subjects from Boston who had experienced childhood lead poisoning 20 to 35 years previously. Of the original 165 subjects, 139 were located and 42 were tested for renal function. Only 6 subjects showed mild signs of renal dysfunction. Other studies of adults and adolescents that had experienced childhood lead poisoning 11 to 23 years previously found no evidence of renal dysfunction (Chisholm, 1971; Moel and Sach, 1992). Loghman-Adham (1998) evaluated renal function in 134 children and young adults, 8 to 13 years after chelation therapy for severe childhood lead poisoning. While there was no evidence of hypertension or impaired kidney function, increased urinary α-amino nitrogen concentrations were observed. Also, 70% of the subjects had aminoaciduria, and 24% had glycosuria. Thus, it was concluded that a partial Fanconi syndrome can persist up to 13 years following childhood lead poisoning. Recent studies have found evidence of renal tubular dysfunction in children living in the vicinity of lead smelters (Bernard *et al.,* 1995; Verberk *et al.,* 1996).

The potential for lead to impair neurobehavioural development in children is the subject of much concern. Lead was reported to cross the placental barrier and be present in the umbilical cord at a concentration of 80 to 90% of that in maternal blood (Inouye, 1989). In general, epidemiological studies of the relationship between PbB levels and neurotoxic effects in the pre- and post-natal child's brain are hampered by the complexity of mental developmental processes, and the questionable sensitivity and significance of IQ tests in detecting subtle differences in neuropsychologic performance. Therefore, despite the large number of epidemiological studies that associate lead exposure with neurotoxicity (some of which are briefly described below), it is not possible to make definitive conclusions regarding potential adverse effects associated with PbB concentrations of less than 25 µg/dL.

Needleman *et al.* (1979) estimated lead exposure from concentrations measured in the dentine of deciduous teeth in a cross-section of first and second graders in 2 Massachusetts communities (n=270). The neuropsychological performance of each child was evaluated using a number of tests including the Wechsler Intelligence Scale for Children - Revised (WISCR). The high dentine lead children performed significantly worse on the Full Scale and Verbal Subscale of the WISCR, with verbal and auditory processing, attention and classroom behaviour being the most sensitive indicators. Needleman *et al.* (1990) followed up on their earlier study to determine whether the neurological deficits observed in the first study persisted into adolescence. The subjects in this study differed from those in the previous study in a number of ways; 10 potential confounding variables were controlled for in this analysis. Needleman *et al.* (1990) determined that those subjects with 1979 dentine lead concentrations above 20 ppm had a higher risk of failing to graduate from high school,

of having a reading disability, lower class marks, greater absenteeism, and decreased vocabulary and reading skills. The authors concluded that the early exposure to lead had an enduring effect on children.

Recently, the Needleman studies have been the subject of controversy. Criticisms of the statistical analysis include improper control of confounding variables, improper exclusion of data such that groups of cases from the original sample of children tested were systematically excluded, and failure to give adequate consideration to the issue of multiple comparisons in the analysis of a large number of variables. Furthermore, there has been some difficulty in obtaining copies of the original data for peer review (Ernhart and Scarr, 1991). In a review of health effects from exposure to low concentrations of lead, Needleman and Bellinger (1991) presented a convincing argument implicating low PbB concentrations and numerous neurobehavioural effects on infants and children.

Decreased IQ values among children with PbB concentrations from 5.6 to 25 µg/dL have been reported (Yule *et al.*, 1981; Fulton *et al.*, 1987; Hatzakis *et al.* 1987). Cooney *et al.* (1989) reported that at PbB concentrations of 0.25 µg/dL, there were no adverse effects on neurobehavioural development. Several authors suggest a LOAEL of 10 to 15 µg/dL for perinatal PbB concentrations (Wolf *et al.*, 1985; Bellinger *et al.*, 1987; Dietrich *et al.*, 1987; Wigg *et al.*, 1988).

Bellinger *et al.* (1987) conducted a prospective cohort study of children (n=249) living in the Boston area, from birth to 2 years of age. While postnatal exposure was not associated with detrimental effects, prenatal exposure was reported to impair early cognitive development [assessed using the Bayley Mental Development Index (MDI)]. In a follow-up to the Boston prospective study, Bellinger *et al.* (1991) found that prenatal PbB concentrations ≥10 µg/dL in cord blood was associated with a slower cognitive development in children up until at least 2 years of age. After 57 months of age, however, prenatal exposure was not related to intelligence test results.

Dietrich *et al.* (1987) investigated the effects of chronic low to moderate fetal lead exposure in lead-hazardous areas of Cincinnati (n=305). A direct relationship between prenatal, umbilical and newborn PbB concentrations and deficits on the Bayley MDI at either 3 or 6 months was observed. Male infants and infants from the poorest families were especially sensitive to lead. However, once the regression analysis was adjusted for confounding variables, no significant effects of fetal lead exposure on the Bayley Psychomotor Developmental Index (PDI) were found. Further study suggested that the neurobehavioural deficits were partly mediated by lead-related reductions in birth weight and gestation. However, a follow-up study found that even after adjustments were made for confounding variables, there remained a statistical significance between postnatal lead blood concentrations of ≥10 µg/dL and lowered Performance IQ when compared to children with mean blood concentrations <10 µg/dL (Dietrich *et al.*, 1993).

A study of the effect of environmental exposure to lead was conducted on a cohort of 537 children born near a lead smelter, near Port Pirie in South Australia (McMichael *et al.*, 1988). Results of this study showed that child development at ages 2, 3, and 4 appeared to be inversely related to postnatal PbB concentrations based on the McCarthy Scales of Children's Abilities. Reductions in perceptual performance and memory scores were also reported. The authors cautioned that the data was somewhat equivocal due to the difficulties in defining and controlling for confounding variables and effects. In a follow-up study, an increase in PbB concentration from 10 to 30 µg/dL was shown to cause a decrease in the General Cognitive Index score on the McCarthy Scales (combines scores for verbal, perceptual-performance, and memory and motor performance subscales) for girls and boys (McMichael *et al.*, 1992). A significantly stronger inverse relationship between PbB concentrations and children's intelligence scores was observed for girls compared to boys.

No relationship was evident between PbB concentrations and child development in a cohort of 260 disadvantaged preschool children in the Cleveland, Ohio area (Ernhart and Greene, 1990). Variables related to the caretaking environment of the children seemed to have the greatest influence on development (*e.g.*, maternal alcohol consumption). A neuropsychological study of 162 Danish school children with elevated dentine lead concentrations demonstrated significantly lower scores on the Wechsler Intelligence Scale for Children (especially on the Verbal IQ and Full Scale IQ), the Bender Visual Motor Gestalt Test, and on a behavioural rating scale (Hansen *et al.*, 1989).

The association between the physical and behavioural characteristics of infants, and maternal and umbilical cord PbB concentrations was investigated among a sample of 42 mother-baby pairs from a heavily industrialized area of Mexico (Rothenberg *et al.*, 1989). As maternal lead concentrations at birth increased, the consolability and self-regulating behaviour of the infants was decreased for as long as 30 days after birth. Increased maternal PbB concentrations were also associated with decreased gestational age.

A cohort of infants from Cincinnati (whose mothers had high PbB concentrations during pregnancy) were followed from birth to age 15 months. A statistically significant negative correlation between PbB concentrations in infants and growth rate was observed (Shukla *et al.*, 1989). Infants who had a 10 µg/dL or greater PbB concentration during the 3- to 15-month age period were approximately 2.0 cm shorter in height at 15 months than infants who had a <10 µg/dL PbB concentration, even though both sets of infants were born to mothers with pre-natal blood concentrations greater than 7.7 µg/dL.

Kindergarten-aged children in the vicinity of a battery recycling smelter in Taiwan had PbB concentrations of 15 to 25 µg/dL, and showed a mild but significant decrease in IQ, compared to kindergarten children from a reference area (Wang *et al.*, 1998). Average air concentrations in the kindergarten classroom were >10 µg Pb/m^3 and nearby soil samples were as much as 400 times greater than background lead concentrations. A follow-up study conducted 2.5 years after children moved away from the smelter area showed a significant decrease in PbB concentrations and partial recovery of IQ.

A European multi-center study on lead neurotoxicity in children conducted by the World Health Organization, Regional Office for Europe (WHO/EURO), and the Commission of the European Communities (Winneke *et al.*, 1990) noted that neurobehavioural effects of environmental lead exposure in children represent weak signals in a noisy background. Consequently, many published cross-sectional studies suffer from insufficient power to detect subtle effects. School-aged children (with PbB concentrations of <5 to 50 µg/dL) were found to have detectable exposure-related behavioural and cognitive effects. However, no threshold for neurotoxicity in school-aged children could be identified from the data.

A report to the U.S. Congress on childhood lead poisoning in the U.S. (Mushak *et al.*, 1989) indicates that PbB concentrations of 10 to 15 µg/dL are associated with a number of adverse health effects, including alterations in neurobehavioural development and electrophysiological function, disturbances in haem biosynthesis, and deficits in growth and maturation. Such effects may occur both prenatally and later in childhood.

A more recent review of a number of cross sectional and prospective cohort studies which investigated neurobehavioural aspects of lead neurotoxicity in children was conducted by Winneke and Krämer (1997). Neurobehavioural deficits in environmentally exposed children were found to occur at PbB concentrations as low as 10 to 15 µg/dL. Based on meta-analyses conducted on the data from both cross sectional and prospective studies, it was concluded that a doubling of PbB concentration from 10 to 20 µg/dL is associated with an average loss of 1-3 IQ points. This was also the conclusion reached by Pocock *et al.* (1994) and WHO (1995). The IQ measure has been the preferred endpoint in the vast majority of epidemiological studies on the effects of lead exposure in children. This endpoint has good psychometric qualities, is well standardized, and is relatively simple to measure in a public health context (Winneke and Krämer, 1997). However, it has been noted that the focus on IQ has interfered with efforts to identify more specific lead-induced functional deficits by means of more detailed neurobehavioural analyses (Bellinger, 1995). For example, some neuropsychological findings in lead-exposed children suggest that part of the impairment resembles performance deficits characteristic of children with attention deficit disorder (Winneke and Krämer, 1997).

4.4.3 Exposure Limit

The U.S. EPA (1998) has classified lead as a probable human carcinogen based on sufficient animal evidence. However, the Carcinogen Assessment Group (U.S. EPA, 1998) did not recommend derivation of a quantitative estimate of oral carcinogenic risk, due to a lack of understanding pertaining to the toxicological and pharmacokinetic characteristics of lead. In addition, the neurobehavioural effects of lead in children were considered to be the most relevant endpoint in determining an exposure limit.

Most of the available information on the potential adverse effects of lead in humans is based on relationships between PbB concentrations and in some cases, dentine lead concentrations, and the various health effects observed. These parameters are accepted because of the lack of

alternate data and the differences in lead absorption between oral, inhalation and dermal exposure routes (Nutrition Foundation, 1982). The actual rates of exposure where adverse human health effects are known to occur are presently unknown.

Based on an analysis of the data generated by Bellinger *et al.* (1987, 1991), Dietrich *et al.* (1987, 1993), Ernhart and Greene (1990), McMichael *et al.* (1988), and Cooney *et al.* (1989), it has been concluded that lead exposures resulting in PbB concentrations of less than 25 µg/dL do not appear to be associated with neurobehavioural deficits in children (Volpe *et al.*, 1992). Inconsistencies were noted in these studies however, and common analyses should be conducted to address and examine these inconsistencies (Volpe *et al.,* 1992). A PbB concentration of 10 µg of lead/dL was the NOAEL determined by Hernberg (1980) and the Nutrition Foundation (1982) based on blood concentrations of FEP in adults. This corresponds to the lower end of the range where no neurotoxicological effects have been reported and where effects on the enzyme systems involved with haemoglobin synthesis are reversible. However, some authors (*e.g.*, Mushak *et al.*, 1989) have observed marginal behavioural effects at PbB concentrations of 15 µg/dL.

Health Canada (1996) recommended a provisional tolerable daily intake (PTDI) for lead of 3.57 µg/kg body weight/day. This value was based on technical reports from annual meetings of the Joint FAO/WHO Expert Committee on Food Additives (JEFCA), and epidemiological studies associating lead exposure with neurological effects in infants and children.

The Ontario Ministry of the Environment and Energy recommended an IOC_{pop} (intake of concern for populations) of 1.85 µg/kg body weight/day which incorporated the population-based significance of the health effects and attempted to minimize the predicted number of children with individual blood lead levels of concern (OMOE, 1996). Subclinical neurobehavioural and developmental effects were the critical effects appearing at the lowest levels of exposure (OMOE, 1994). The IOC_{pop} was based on an LOAEL in infants and young children of 10 µg/dL, converted to an intake, with an applied uncertainty factor of 2 for the use of an LOAEL (OMOE, 1994). Because the IOC_{pop} was intended for the entire population and independent of route of exposure, 1.85 µg/kg body weight/day was adopted for both oral and inhalation exposure limits for the current assessment.

For the purpose of this assessment, the human bioavailability was assumed to be 10 to 15% for adults, and 42 to 53% for children/adolescents for ingestion, 19 to 22% for adults, and 38.2 to 44.8% for children/adolescents for inhalation, and 0.06% for dermal exposure.

4.4.4 References

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PART 4.5
TOXICOLOGICAL REVIEW: NICKEL

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4.5.0 TOXICOLOGICAL REVIEW: NICKEL

4.5.1 Fraction Absorbed *Via* Different Routes

4.5.1.1 Fraction Absorbed Via Ingestion

Ingestion is a major route of exposure for nickel compounds (U.S. EPA, 1986; Nieboer and Nriagu, 1992). The different chemical forms of nickel can significantly influence the amount of nickel that is absorbed from the gastrointestinal tract (U.S. EPA, 1986). For example, metallic nickel, nickel oxide and nickel subsulfide are poorly absorbed when ingested (ITER, 1998). Estimates of nickel bioavailability following ingestion vary from study to study and have been reported to range from 1 to 30% (Perry and Perry, 1959; ICRP, 1960; Nodiya, 1972; Horak and Sunderman, 1973; Christensen and Lagesson, 1981; Hansen and Tjell, 1981; Owen, 1990). After an overnight fast, human subjects orally dosed with 12, 18, and 50 µg/kg body weight had absorbed a mean of 27 ± 17% of the dose when ingested in water and 0.7 ± 0.4 % of the dose when ingested in food (Sunderman *et al.*, 1989). Four healthy human subjects (two males; two females) ingested 10 µg/kg body weight nickel as stable ^{62}Ni isotope in water after overnight fasting. The percentage of ^{62}Ni absorbed ranged from 29 to 40% (mean of approximately 33%), based on calculation of the amount of ^{62}Ni excreted in the feces (Patriarca *et al.*, 1997). A mouse study concluded that 1 to 10% of nickel is absorbed after oral administration of nickel (by stomach tube) in the form of nickel sulphate hexahydrate or nickel chloride solutions (ATSDR, 1992; Nielsen *et al.*, 1993). This range had also been previously reported by the U.S. EPA (1986). Therefore, for the current exposure assessment, the oral bioavailability was assumed to range from 1 to 10%.

4.5.1.2 Fraction Absorbed Via Inhalation

The U.S. EPA (1986) concluded that nickel was poorly absorbed from the lungs, and noted that there was very little data regarding pulmonary absorption of deposited nickel in humans. Reports of nickel absorption *via* inhalation range from 6% (Owen, 1990) to 40% (ICRP, 1960). Given the wide range of inhalation bioavailability estimates in the literature, the inhalation bioavailability for this assessment was based on the airborne particle dynamics model. Based on this model, about 13% of airborne particulates would enter the lungs and thus 13% of particulate-bound nickel would be bioavailable in the lung. Approximately 60% of airborne particles would be cleared by the mucociliary apparatus and swallowed, and of this, 1 to 10% would be absorbed from the gastrointestinal tract, resulting in an additional 0.6 to 6% absorption. Therefore, the total bioavailability of airborne nickel from particles was assumed to range from 13.6 to 19% (13% from the respiratory system plus 0.6 to 6% of the cleared material).

4.5.1.3 Fraction Absorbed Via Dermal Exposure

A report of the National Cancer Institute (NCI, 1985) concluded that the absorption of nickel into the blood through skin had not been demonstrated in humans, as nickel uptake was

limited to the outer layers of skin (NCI, 1985; U.S. EPA, 1986). A study in which radioactive nickel was applied to occluded human skin reported dermal uptake ranging from 55 to 77% for nickel sulphate (Norgaard, 1955); however, it could not be determined if the nickel was absorbed into the bloodstream or merely into the deep layers of the skin (ATSDR, 1997). Less than 1% of nickel chloride was absorbed through the skin of guinea pigs within 24 hours (Lloyd, 1980). For the current assessment, the amount of nickel absorbed through dermal exposure was assumed to be similar to that of inorganic lead (*i.e.*, 0.06%). This value was selected for this assessment as the predominant potential dermal exposure to nickel would be in the form of particulate-bound nickel within a soil-like matrix.

4.5.2 Health Hazard Assessment

4.5.2.1 Genotoxicity and Mutagenicity

A number of nickel compounds have been demonstrated to have both genotoxic and mutagenic properties. Insoluble crystalline nickel compounds are more active in genetic toxicity assays than soluble or amorphous forms of nickel (NTP, 1996a). Nickel compounds produced chromosomal aberrations *in vitro* in Chinese hamster ovary cells (Sen and Costa, 1985) and nickel chloride induced mutation affecting RNA splicing during expression of a specific gene (Chiocca *et al.*, 1991). Rossetto *et al.* (1994) found that soluble nickel compounds produced gene deletions after *in vitro* exposures of a transgenic Chinese hamster ovary cell line (AS52) containing a bacterial gene substitute for the mammalian HGPRT gene. Mutagenesis of several insoluble nickel compounds including crystalline nickel sulfide, nickel subsulfide, and nickel oxides (black and green) has been demonstrated using the HGPRT gene of the well-defined V79 cell line, and in two transgenic derivative cell lines of V79 (Kargacin *et al.*, 1993). One of the transgenic cell lines responded to the insoluble Nickel compounds by the production of site specific mutagenesis. In V79 cells however, NiS and NiO (black) did not induce a mutagenic response in the HGPRT gene (Kargacin *et al.*, 1993).

Nickel compounds have been shown to cause cell transformation in a number of primary cell cultures. Transformation by NiO has been shown in Syrian hamster embryo cells (Costa *et al.*, 1981; Sunderman *et al.*, 1987), and rat tracheal epithelial cells (Patierno *et al.*, 1993) and a number of other established cell lines (Hansen and Stern, 1983). Sunderman *et al.* (1987) reported the results of cytotoxicity and cell transformation in *in vitro* assays using Syrian hamster embryo (SHE) treated with a series of nickel oxides. Ten forms of NiO (bunsenite) with or without CuO (tenorite) as part of the mineral preparation were examined. The results of the SHE transformation assays showed that as the purity of the NiO species increased, the ability for metal particulate to induce cell transformation was lost. The presence of traces of sulfur or copper resulted in an increase in the frequency of cell transformation. Calcination of black NiO (dissolution half life 0.8 yr) by treatment at temperatures from 735 °C to 1045 °C progressively decreased solubility and reduced the biological activity of the oxides both *in vitro* and *in vivo* (Sunderman *et al.*, 1987). In general, the results of genotoxicity assays *in vitro* using NiO have given variable results. The presence of contaminants such as

sulfur or copper influences the solubility and reactivity of Ni (II) in these assays. This may explain why NiO is not able to induce chromosomal aberrations in human lymphocytes *in vitro* (Paton *et al.*, 1972; Kanematsu *et al.*, 1980). However, in sensitive cell transformation assays, nickel oxides appear to be capable of inducing changes in several cell lines *in vitro* (Hansen and Stern, 1983; Hansen and Stern, 1985; Biederman and Landolph, 1987; Patierno *et al.*, 1993). Fletcher *et al.* (1994) suggested that NiO produced mutations in AS52 cells, but that neither black NiO nor green NiO showed a clear dose response relationship for mutation as has been demonstrated for several soluble nickel compounds. Analysis of the nickel content of the cytosol and nuclei of cells grown in tissue culture revealed significant concentrations of both forms of NiO in cell cytosol, but evidence for significant concentrations in the nuclei was somewhat less certain. This suggests that NiO may not reach the nucleus in sufficient concentrations to produce a mutagenic response in cultured AS52 cells. Fletcher *et al.* (1994) concluded that NiO produces mutations in *in vitro* experiments at frequencies only slightly above background, suggesting that this form of nickel is weakly mutagenic, if at all. While the evidence for positive genotoxicity is supported by data from cell transformation assays, it appears that in some cases, contamination of the NiO with traces of sulfur or other metal oxides may have been responsible for the results observed.

An *in vivo* study using Sprague-Dawley rats exposed to nickel chloride at a dose of 44 mg/kg body weight found evidence of DNA strand breaks in hepatic cells 4 hours post-treatment (Stinson *et al.*, 1992). However, this dose was acutely toxic and resulted in mortality within 48 hours. At a lower dose of approximately 34 mg/kg body weight, no DNA strand breakage was observed in hepatic cells. An NTP study with NiO (NTP, 1996c) found no evidence for micronucleus induction *in vivo*; however, this result is not unexpected given both the lack of solubility of NiO and the likelihood that the particulate material could not reach the hematopoietic system to any significant extent. Şaplakoğlu *et al.* (1997) subcutaneously injected male albino rats with nickel chloride at a dose of 44 mg/kg body weight. They observed no DNA strand breaks in the liver. However single strand DNA breakage was observed in lung and kidney cells. Lung tissue was the most susceptible to DNA stand breakage. Male F344 rats administered a single intraperitoneal injection of 90 µmol nickel acetate/kg body weight were assayed for DNA base damage for up to 14 days post-treatment (Kasprzak *et al.*, 1997). Ten different damaged bases were quantified, with the DNA damage becoming significant from day 1 post-treatment. The magnitude and persistence of the base damage was organ and base-dependent. In the liver, levels of 5 damaged base products were significantly elevated over controls, while levels of 3 damaged base products were elevated in the kidney. As the levels of damaged base products persisted longer in the kidney than the liver for the duration of the study (14 days), the authors speculated that the nickel-induced oxidative DNA base damage may be associated with the susceptibility of the rat kidney to nickel-initiated carcinogenesis.

Werfel *et al.* (1998) measured DNA damage (by alkaline filter elution) and SCE frequencies in the lymphocytes of 39 welders occupationally exposed to chromium and nickel and 39 control subjects. Welders showed a significantly higher rate of single strand DNA breaks and

significantly elevated SCE frequency. The average concentration of nickel in the blood of these welders was 4.6 µg/L. The authors estimated that this blood concentration corresponded to an average nickel air concentration of 300 µg/m^3. The results of this study however, did not agree with previous studies conducted with lymphocytes from welders. Decreased SCE frequencies in lymphocytes of welders (relative to controls) were observed by Knudsen *et al.* (1992), Jelmert *et al.* (1995), and Popp *et al.* (1991). There is presently much uncertainty regarding the nature of the interaction between chromium and nickel, and whether there are dose-dependent effects of nickel on DNA strand breaks and SCE frequencies.

Although there are conflicting study results for some nickel compounds, the available genotoxicity and mutagenicity data strongly suggest that nickel compounds are genotoxic and mutagenic. Therefore, for the current assessment, nickel was considered to be both genotoxic and mutagenic.

4.5.2.2 Animal Studies

Dermal acute toxicity studies of nickel compounds indicate a potential for nickel sulphate hexahydrate to cause cutaneous injury and lipid peroxidation in guinea pigs at a dose of 50 mg/kg/day for 7 to 14 days (Mathur *et al.*, 1992). Nickel sulphate has also been shown to act as a contact allergen in mice (Ikarashi *et al.*, 1992).

Several subchronic studies have been conducted to investigate the effects of inhalation treatment with various species of nickel on rats and mice (Bingham *et al.*, 1972; Dunnick *et al.*, 1989; NTP, 1996a,b,c). Bingham *et al.* (1972) observed increased numbers of alveolar macrophages following exposure to nickel oxide, and microscopic changes in the lungs following exposures to nickel oxide and nickel chloride in rats. Dunnick *et al.* (1989) exposed rats and mice to nickel subsulphide, nickel sulphate hexahydrate and nickel oxide 6 hours/day, 5 days/week for 13 weeks. These authors reported changes in body weight in rats in several dose groups in the nickel subsulphide treated animals. Treatment-related effects included increases in lung weight, as well as histopathological changes in the lung, nasal cavity and bronchial lymph node, such as alveolar macrophage hyperplasia, inflammation and fibrosis, which increased in severity with increasing exposure concentration. In rats, NOAEL values for respiratory tract lesions were determined to be 0.05 mg/m^3 for nickel sulphate, and 0.9 mg/m^3 for nickel oxide. In mice, the NOAELs for nickel sulphate, subsulphide and oxide were 0.1, 0.4, and 2 mg/m^3, respectively.

Experimental Animal Carcinogenicity Studies

Numerous carcinogenicity experiments have been conducted with nickel compounds, administered *via* injection, inhalation or ingestion. Recent chronic inhalation studies have clearly indicated that different nickel compounds have different carcinogenic potentials and different animal species show different carcinogenic responses to various nickel compounds (NTP, 1996a,b,c).

Intrarenal injection of nickel subsulphide was reported to result in an increased incidence of renal tumours in male Fischer 344/NC rats (Higinbotham *et al.*, 1992); an increase in K-ras mutations was associated with the tumours, and was considered to provide initiation for the carcinogenic effects. Intrarenal administration of nickel subsulphide to male Fischer 344 rats was associated with an increase in kidney tumours, as well as a transient but significantly increased erythrocytosis (Sunderman *et al.*, 1990). Oncogene amplification was implicated in 2 of the 6 tumours based on DNA hybridization assays. Injection studies of several nickel compounds have indicated a potential for the induction of distal tumours. Nickel acetate was reported to induce a significant increase in lung tumours in rats following a series of intraperitoneal injections (Stoner *et al.*, 1976). Similarly, Lau *et al.* (1972) observed an increased incidence of malignant tumours at various sites following intravenous administration of nickel carbonyl.

A number of inhalation studies of nickel carcinogenesis have yielded positive results. Ottolenghi *et al.* (1974) exposed Fischer 344 rats to 0.97 mg nickel sulphide/m^3 for 6 hours/day, 5 days/week for 78 weeks. Towards the end of treatment, an increase in mortality and a decrease in body weight was observed. An increased incidence of lung tumours was observed during treatment and during a 30-week observation period. Nickel sulphide-treated rats developed 29 tumours and 10 adenocarcinomas compared to control responses of 2 and 1, respectively. Sunderman *et al.* (1957, 1959) also observed increased incidences of lung tumours in rats exposed to nickel carbonyl, at concentrations of 30 µg/L for 52 weeks or a combination of 30 and 60 µg/L, for 3 and 49 weeks, respectively. The U.S. EPA (1986) chose the study by Ottolenghi *et al.* (1974) in the determination of a q1* value representing the risk of lung carcinogenesis arising from inhalation of nickel sulphide. The unit risk values, calculated using 3 different models, ranged from 1.8×10^{-3} to 6.1×10^{-3} $(\mu g/m^3)^{-1}$ (U.S. EPA, 1986), with an average unit risk value of 3.88×10^{-3} $(\mu g/m^3)^{-1}$.

More recently, 3 chronic inhalation studies have been published by the National Toxicology Program (NTP, 1996a,b,c). This series of studies involved 16-day, 13-week and 2-year inhalation exposures to nickel subsulphide, nickel sulphate hexahydrate and nickel oxide. For the purposes of this assessment, a summary is provided only for the chronic component (*i.e.*, 2-year portion) of each study.

In the nickel subsulphide inhalation study (NTP, 1996a), rats were treated with 0, 0.11, or 0.73 mg Ni/m^3 and mice with 0, 0.44 or 0.88 mg Ni/m^3, 6 hours/day, 5 days/week for 104 weeks. The nickel subsulphide used in this study was in the form of high purity nickel subsulphide powder from which a fluid bed generated aerosol was produced. The survival rate of all treated animals was comparable to that of the controls. The mean body weights of high dose rats and all treated mice were lower than the controls. Rapid and shallow breathing was noted in treated rats as well as laboured respiration following exposure periods in mice. Some haematological changes including an elevated haematocrit were noted in treated animals. An increased incidence of non-neoplastic effects including chronic active inflammation and macrophage hyperplasia was noted in low dose rats and mice. There was an increased incidence of alveolar/bronchiolar adenoma or carcinoma or squamous cell

carcinoma in male and female rats, benign or malignant pheochromocytoma in males and benign pheochromocytoma in female rats. There was no evidence of carcinogenic activity in mice.

In the nickel sulphate hexahydrate study (NTP, 1996b), rats were exposed by inhalation to 0, 0.03, 0.06 or 0.11 mg Ni/m^3, 6 hours/day, 5 days/week for 104 weeks, in the form of a nickel sulphate hexahydrate aerosol generated from aqueous solution. The survival rates of all exposed rats were similar to those of the controls. Final mean body weights of all exposed groups of male rats and 0.03 and 0.06 mg Ni/m^3 females were similar to those of control rats. No treatment related haematological differences were noted. The incidences of chronic active inflammation, macrophage hyperplasia, alveolar proteinases and fibrosis were significantly increased in the medium and high dose male and female rats. There was no evidence of carcinogenic activity. The NOAEL for rats was estimated to be 0.03 mg Ni/m^3 or 0.028 mg Ni/kg body weight/day (0.03 mg/m^3 x 0.36 m^3/day ÷ 0.38 kg).

In the same nickel sulphate hexahydrate study (NTP, 1996b), mice were treated with 0, 0.06, 0.11 or 0.22 mg Ni/m^3 according to the same protocol used for the rats. The survival rate of all exposed mice were similar to those of the controls. The mean body weights of high dose males and all treated female mice were lower than those of the controls. No treatment-related haematological differences were noted. The incidences of chronic active inflammation, bronchiolization, and macrophage hyperplasia were significantly increased in the medium and high dose males and all females. There was no evidence of carcinogenic activity. The NOAEL for male and female mice was determined to be 0.06 mg Ni/m^3 or 0.10 mg Ni/kg body weight/day (0.06 mg Ni/m^3 x 0.063 m^3/day ÷ 0.0373 kg), the lowest dose tested.

In the nickel oxide inhalation study (NTP, 1996c), rats were treated with 0, 0.5, 1.0, or 2.0 mg Ni/m^3 and mice with 0, 1.0, 2.0, or 3.9 mg Ni/m^3, 6 hours/day, 5 days/week for 104 weeks. The nickel oxide exposure in this study was in the form of very pure high temperature green nickel oxide aerosol, generated from fluid bed generators. The survival rate of all treated animals was comparable to that of the controls. Mean body weights of high dose male rats and medium and high dose female rats were slightly lower than controls; high dose female mice body weights were also slightly lower than controls. No treatment related haematological differences were noted at the 15-month interim evaluation. An increase in the incidence of chronic inflammation and bronchial lymphoid hyperplasia was noted for low dose rats. An increase in the incidence of lung bronchiolization, proteinases, and chronic inflammation was noted in the low dose mice. There was some evidence of an increased incidence of alveolar/bronchiolar adenoma or carcinoma or squamous cell carcinoma, and benign or malignant pheochromocytoma in rats. There was no evidence of carcinogenic activity in male mice but equivocal evidence of alveolar/bronchiolar adenoma or carcinoma in female mice. The LOAEL for rats was determined to be 0.5 mg Ni/m^3 or 0.47 mg Ni/kg body weight/day (0.5 mg Ni/m^3 x 0.36 m^3/day ÷ 0.38 kg).

The authors of the nickel oxide NTP study concluded that there was some evidence of carcinogenic activity in both male and female rats. The weight of evidence for pure NiO

carcinogenicity indicates that it is not likely acting through a mutagenic process but rather as a threshold carcinogen. In light of this data it can be concluded that the observed rat lung tumours were the result of threshold mechanisms involving tissue damage secondary to an inflammatory response. In addition, the adrenal tumours were concluded to be an indirect effect of the chemical, possibly related to stress. It must be noted that there are substantial differences between rats and humans in the incidence of spontaneous and induced adrenal medullary lesions, and in the morphology and physiology of the lesions themselves. Adrenal medullary tumours, induced in rats, particularly for the F344 strain, may be species- and strain-specific and of little or no relevance to humans (Lynch *et al.*, 1996).

The authors of the nickel oxide NTP study also concluded that there was equivocal evidence of carcinogenic activity in the lungs of female mice. As outlined in the subcommittee comments section of this report (NTP, 1996c), there was some degree of disagreement surrounding this issue. While one reviewer (Dr. J. Reddy) contended that there was some evidence of carcinogenic activity in female mice, a second reviewer (Dr. J. Ward) pointed out that there was no dose response relationship and felt that the appropriate conclusion should have been no evidence of carcinogenicity.

Thus, there appears to be a threshold of exposure for NiO induced carcinogenicity. This conclusion is supported by the fact that there is little data to support differences in uptake and/or intracellular metabolism of nickel oxide between rats and mice. This suggests that patterns of carcinogenicity in response to a genotoxic, non-threshold carcinogen should be similar for both rodent species. The observation that exposure to nickel oxide demonstrates some evidence of carcinogenicity in rats and no evidence in mice at comparable doses is not consistent with what would be predicted for a non-threshold carcinogen. In addition, no tumours of the respiratory system were noted in treated rats at either of the interim evaluations, which is once again inconsistent with the profile of a non-threshold complete carcinogen. Furthermore, no lung tumours were observed in rats at the low dose of 0.5 mg Ni/m^3, which again is indicative of a threshold mechanism secondary to inflammation.

In contrast to the nickel oxide study, no tumours were observed in rats or mice in the nickel sulphate hexahydrate study, in spite of positive trends of an inflammatory response in the lungs of treated animals. The authors interpreted this finding by noting that the differences between severities of lung inflammation lesions in exposed and control rats in the nickel oxide and nickel subsulphide studies were greater than the differences between severities of exposed and control rats in the nickel sulphate hexahydrate study. In addition, nickel oxide and subsulphide treated rats had significant parenchymal damage secondary to inflammation, supportive of the conclusion that the lung tumours observed in the nickel oxide study represented a threshold response involving chronic inflammation and tissue damage. This conclusion is consistent with the interpretation of Oller *et al.* (1997) who conducted a detailed review of available *in vitro* and *in vivo* studies related to the carcinogenicity of nickel compounds.

Ingestion of nickel compounds has not been associated with increased tumourigenesis, when administered in the diet or in drinking water. Three long-term drinking water studies were conducted using only 1 dose level. Schroeder *et al.* (1964) and Schroeder and Mitchener (1975) exposed Swiss mice to nickel acetate. Schroeder *et al.* (1974) exposed Long-Evans rats to an unspecified species of nickel. No neoplastic activity was observed in any of these studies.

Ambrose *et al.* (1976) reported data on rats (25/sex/group) and dogs (3/sex/group) exposed for 2 years to nickel sulphate hexahydrate in the diet at 100, 1,000, and 2,500 ppm (equal to 5,000, 50,000 and 125,000 µg/kg body weight/day for the rat, assuming a body weight of 0.350 kg and food consumption of 17.5 g/day). Non-neoplastic effects included decreased growth in dogs (mid and high doses) and rats (high dose), alterations in blood and urinary chemistry in high-dose dogs, and changes in relative organ weights for mid and high dose female rats (heart and liver) and high dose dogs (kidney and liver). No significant histopathological effects were noted in rats. No significant histopathological findings were reported for the low and mid dose dogs, while high dose dogs had cholesterol granulomas of the lung. The NOAEL was estimated to be 5,000 µg Ni/kg body weight/day, based on the non-neoplastic changes in the rat. The authors acknowledged that the 2-year rat survival was poor, particularly in the control groups. However, the NOAEL of this chronic study (5,000 µg Ni/kg body weight/day) is consistent with the NOAEL of 5,000 µg Ni/kg body weight/day determined from a similar 90-day gavage study (ABC, 1986; U.S. EPA, 1998).

Reproductive and Developmental Toxicity

A 3-generation study, carried out by Ambrose *et al.* (1976), noted a higher incidence of stillborns in the first generation of albino rats fed 250, 500, or 1,000 ppm nickel in their diet (nickel sulphate hexahydrate) and depressed body weights of weanlings on the 1,000 ppm diet in all generations. A higher incidence of stillborns was not observed in subsequent generations (Ambrose *et al.*, 1976). The U.S. EPA concluded that this study had some statistical design limitations and concluded that a NOAEL could not be clearly defined (U.S. EPA, 1998).

Schroeder *et al.* (1974) administered 5 ppm nickel in drinking water (equivalent to 0.3 mg/kg body weight) to weanling rats for their remaining lifetime and observed no adverse effects on growth or survival (Health Canada, 1994). A 3-generation study in rats exposed to nickel in their food and drinking water at concentrations of 0.31 ppm and 5 ppm, respectively, displayed declining litter sizes with each successive generation (Schroeder and Mitchener, 1971). More treated young rats died in each generation relative to the control rats and significant numbers of runts occurred in the F1 and F3 generations. The total dose of nickel administered to these rats from food and drinking water is equivalent to 0.32 mg/kg body weight/day (Health Canada, 1994); only 1 dose was included in this study. The U.S. EPA criticized this study on the basis of the fact that the end result is based on a total of 5 matings and the matings were not randomized nor were the males rotated. In addition, the restricted exposure to other trace metals may have contributed to the toxicity of nickel.

A more recent multigenerational study involved the administration of 0, 10, 50, or 250 ppm of nickel chloride in the drinking water (equivalent to 0, 1.3, 6.8, or 31.6 mg/kg/day) for 11 weeks before mating and then through 2 successive periods of mating, gestation (G1,G2) and lactation (L1,L2) (Smith *et al.*, 1993; Health Canada, 1994). A reduction in maternal weight gain during G1 in the mid- and high-exposure groups was observed. Also, the proportion of dead pups per litter was significantly elevated at the high dose in L1 and at 10 and 250 ppm, but not at 50 ppm in L2. Health Canada concluded that the LOAEL of this study was equal to 10 ppm or 1.3 mg/kg/day (Health Canada, 1994). However, the U.S. EPA concluded that neither a NOAEL nor a LOAEL could be established due to the lack of a clear dose response relationship (U.S. EPA, 1998).

In a 2-generation study, nickel chloride was administered to rats in drinking water for 90 days before breeding at doses of 0, 50, 250, and 500 ppm. On the basis of organ and body weights, as well as histopathological findings, the NOAEL was reported to be 250 ppm or 30,800 µg/kg/day (RTI, 1987; U.S. EPA, 1998).

4.5.2.3 Human Studies

Nickel is an essential element in all vertebrate animals and humans; however, nickel deficiency has never been reported in humans as nickel intake generally exceeds dietary requirements (Anke *et al.*, 1995). Approximately 10 to 15% of women and 1 to 3% of men living in industrialized countries are sensitized to nickel (Andreassi *et al.*, 1998). Typically, nickel-sensitized individuals suffer from allergic contact dermatitis. Dermal contact with nickel leading to an antigenic response and dermatitis has been well documented in the literature (NAS, 1975; NCI, 1985; U.S. EPA, 1986).

Recent studies have shown that acute oral exposure to nickel compounds can result in flare-ups of allergic contact dermatitis and eczema and in some cases, urticaria and respiratory symptoms in women that are sensitized to nickel (Andreassi *et al.*, 1998; Boscolo *et al.*, 1995).

Extensive reviews of the toxicology of nickel and nickel compounds, including animal carcinogenicity and human epidemiological data, were published by the International Agency for Research on Cancer in 1990 (IARC, 1990), and by Doll *et al.* (1990). The studies reviewed included human exposures associated with nickel mining, smelting, refining and high nickel alloy manufacture, as well as one industry in which pure nickel powder was used. In general, the reviews of these studies indicated increased risks for lung and nasal cancers associated with occupational inhalation exposures incurred during high temperature oxidation of nickel matte and nickel-copper matte (roasting, sintering, calcining), as well as with exposures in electrolytic refining and hydrometallurgy. The reviews also indicated that different classes of nickel compounds have different carcinogenic potencies.

However, the epidemiological studies reviewed by IARC (1990) and Doll *et al.* (1990) had several limitations. The principal limitation of these studies was the lack of data related to

concentrations of nickel in air within the facilities that were studied. Both Doll *et al.* (1990) and IARC (1990) acknowledged that no actual measurements of specific nickel species in work-place air were available. Thus, there were either poor or no data on which to base exposure estimates. Moreover, in many cases, even the total airborne nickel concentration within a given facility or department had to be estimated from surrogate data. Due to the poor quality of the available data, it was not possible to establish dose-response relationships for specific nickel species. In addition, the mechanism underlying the carcinogenic hazard of the various individual nickel species remained to be established. Furthermore, Doll *et al.* (1990) noted that the conclusions of many of the epidemiological studies (with respect to lung tumours) were confounded by a lack of information about the smoking habits of the workers.

The 4 studies used in the U.S. EPA determination of the unit risk associated with nickel are briefly discussed below. The U.S. EPA q1* for nickel refinery dust is equal to 2.4×10^{-4} $(\mu g/m^3)^{-1}$ which results in an RsD of 0.013 µg/kg/day at a risk level of 1/100,000 (assuming a breathing rate of 23 m^3/day and a body weight of 70 kg).

A cohort of employees of a nickel refinery in West Virginia who experienced a minimum 1 year exposure to nickel refinery dusts (containing nickel subsulphide, sulphate and oxide or only nickel oxide) did not show an increased incidence of lung cancer above expected rates (Enterline and Marsh, 1982). Chovil *et al.* (1981) studied a cohort of nickel refinery workers in Ontario, and observed a dose-related trend for the relationship between weighted exposure in years to the incidence of lung cancer. Similarly, a cohort of Welsh nickel refinery workers had elevated risks of cancer compared to the national average. Increased rates of nasal cancer were observed in men employed prior to 1920, while this rate was less than the national average for those starting work between 1920 and 1925, and equalled the expected value for those employed after 1925 (Doll *et al.*, 1977). A significantly increased lung cancer-related mortality was observed in employees starting prior to 1925 but not in those starting between the years 1930 to 1944. Magnus *et al.* (1982) conducted a study of men employed at a nickel refinery in Norway, and reported an elevated occurrence of respiratory cancer for nickel-exposed workers compared to expected values, and for workers involved in nickel processing steps compared to non-processing employees.

Each of these epidemiology studies used in the U.S. EPA determination of the unit risk associated with nickel had a number of limitations. For example, none were able to account for exposures to other chemicals, particularly other metals or other nickel species (such as nickel subsulphide), that were present in the occupational environment of a nickel refinery. Only one study attempted to account for differences between smokers and non-smokers. Three of the 4 studies did not provide measurements of airborne nickel concentrations or estimates of worker exposure. The U.S. EPA estimated exposures based on information provided in other reports in which concentrations of nickel in the work environment were projected on the basis of the operating procedures used. Other problems included poorly or heterogeneously defined cohorts, poor follow-up success, and no consideration of the role of the latency period for lung cancer. Of the 4 studies summarized above, Enterline and Marsh (1982) was the most relevant since estimated exposures were provided, the latent period

could be examined, and the effects in refinery workers could be compared to non-refinery workers. However, the mixed exposure to other substances and to cigarette smoke were confounding factors that limited the interpretation of this study.

The majority of the epidemiological studies described in IARC (1990) and Doll *et al.* (1990) noted an apparent increased occupational risk of lung and nasal cancers for a small proportion of nickel workers. This was also the conclusion from epidemiological studies with workers at the INCO facility in Sudbury, Ontario (Roberts *et al.*, 1989a,b; Muir *et al.*, 1994). Recently, Anttila *et al.* (1998) followed up on an earlier study of lung cancer incidence in workers at a nickel refinery in Harjavalta, Finland (Karjalainen *et al.*, 1992). In this first study, examination of cancer registry data for a cohort of workers followed from 1953 to 1987 revealed an elevated incidence of nasal cancer and a slight increase in lung cancer incidence. Anttila *et al.* (1998) followed up on this study by examining cancer registry data up to the end of 1995. A cohort of 1388 workers employed for at least three months at the copper/nickel smelter and nickel refinery in Harjavalta was studied. Overall cancer incidence in this cohort was similar to the unexposed cohort; both were at expected levels for the Finnish population. A small increase in lung cancer incidence, and an increased risk of nasal cancer in the exposed cohort were observed. Refinery workers were primarily exposed to nickel sulfate at concentrations below 500 $\mu g/m^3$, but exposure to lower concentrations of other soluble nickel compounds also occurred. As the elevated lung and nasal cancer risks were confined to refinery workers, where the primary exposure was to nickel sulfate, the authors concluded that nickel sulfate is likely responsible for the excess cancer risk. An increased risk of stomach cancer in the nickel-exposed cohort was also observed in this study; however, as stomach cancer has not generally been associated with nickel exposure, the authors speculated that this was a chance finding.

4.5.3 Exposure Limits

As indicated in the previous sections, the toxicology of nickel compounds is complex and controversial. This is reflected in the available regulatory exposure limits.

Nickel Refinery Dusts and Nickel Subsulfide

Nickel refinery dusts and nickel subsulfide are both classified by the U.S. EPA as A: human carcinogens. Only inhalation unit risk values for these substances are available. For nickel refinery dusts, the inhalation unit risk is 2.4×10^{-4} $(\mu g/m^3)^{-1}$, which corresponds to a q_1^* of 0.00073 per µg/kg body weight/day (assuming a breathing rate of 23 m^3/day and a body weight of 70 kg) (U.S. EPA, 1998). The studies upon which the unit risk value for nickel refinery dusts are based are briefly described in the previous section. For nickel subsulfide (a major component of nickel refinery dust), the inhalation unit risk is 4.8×10^{-4} $(\mu g/m^3)^{-1}$, which corresponds to a q_1^* of 0.0015 per µg/kg body weight/day (assuming a breathing rate of 23 m^3/day and a body weight of 70 kg) (U.S. EPA, 1998). To date, chronic non-cancer oral and inhalation exposure limits for these substances have not been derived by any jurisdiction in the U.S. However, Health Canada (1996) reports a non-cancer tolerable inhalation

concentration of 0.018 µg/m^3 for nickel subsulfide. Assuming a breathing rate of 23 m^3/day and a body weight of 70 kg, this air concentration would correspond to a tolerable dose of 0.006 µg/kg body weight/day.

Nickel Soluble Salts

While some jurisdictions consider soluble nickel compounds to be human carcinogens (*i.e.*, Health Canada), the available evidence suggests that these compounds behave as threshold chemicals; thus the exposure limit is expressed as an RfD. The U.S. EPA (1986; 1998) recommended an oral RfD of 20 µg/kg body weight/day for soluble salts of nickel based on rat data from the Ambrose *et al.* (1976) study. This RfD was based on a NOAEL for nickel of 5,000 µg/kg body weight/day which corresponded to a dietary concentration of 100 ppm nickel in their diet over the 2-year study. A 300-fold safety factor was applied to the NOAEL of 5,000 µg/kg body weight/day; 10-fold for interspecies differences, 10-fold for sensitive individuals in the population, and 3-fold to account for limitations in statistical design [recommended by the U.S. EPA (1986)].

Although the study was criticized by the U.S. EPA for lacking a clear dose-response relationship, Health Canada (1994) derived a TDI of 1.3 µg/kg body weight/day for nickel chloride, by applying a 1,000-fold uncertainty factor (10-fold for use of a LOAEL, 10-fold for interspecies differences and 10-fold for sensitive individuals in the population) to the LOAEL of 1.3 mg/kg/day based on reproductive toxicity in the rat study by Smith *et al.* (1993).

For nickel sulphate, Health Canada (1996) derived a TDI of 50 µg/kg body weight/day, based on the NOAEL from the Ambrose *et al.* (1976) and using an uncertainty factor of 100 (10-fold for interspecies extrapolation, 10-fold for interspecies variation). Unlike, the U.S. EPA, Health Canada did consider an additional uncertainty factor for design limitations necessary. For the inhalation route, Health Canada (1996) recommends a tolerable inhalation concentration (non-cancer effects) of 0.0035 µg/m^3 for nickel sulphate. Assuming a breathing rate of 23 m^3/day and a body weight of 70 kg, this air concentration would correspond to a dose of 0.0012 µg/kg body weight/day. The RfD was based on lung and nasal lesions in rats and mice observed by Dunnick *et al.* (1989).

Nickel Oxide

Nickel oxide is also considered to behave as a threshold substance. However, no regulatory exposure limits have been derived for the oral or inhalation routes by U.S. agencies (ITER, 1998). Health Canada (1996) recommends a tolerable inhalation concentration (non-cancer effects) of 0.02 µg/m^3. Assuming a breathing rate of 23 m^3/day and a body weight of 70 kg, this air concentration would correspond to a dose of 0.007 µg/kg body weight/day. Health Canada has not derived a chronic oral exposure limit for nickel oxide.

Metallic Nickel

No oral or inhalation, cancer or non-cancer regulatory exposure limits for metallic nickel were identified in the literature reviewed for the current assessment, although Health Canada (1996) reports a provisional non-cancer tolerable concentration (inhalation) of 0.018 $\mu g/m^3$. Assuming a breathing rate of 23 m^3/day and a body weight of 70 kg, this air concentration would correspond to a dose of 0.006 µg/kg body weight/day.

With respect to inhalation exposures of nickel compounds in general, the Ontario Ministry of the Environment (OMOE) recommends a 24-hour reference concentration (RfC) of 2 $\mu g/m^3$ as an acute exposure limit for nickel compounds (OMOE, 1994). The only chronic regulatory inhalation exposure limit identified for nickel is a Minimal Risk Level (MRL) of 0.2 $\mu g/m^3$ (ATSDR, 1998), which when expressed as a dose is equal to 0.07 µg/kg body weight/day (assuming a breathing rate of 23 m^3/day and a body weight of 70 kg).

No regulatory dermal exposure limits for nickel compounds were identified in the literature reviewed for the current assessment.

Recommended Exposure Limits

For the purposes of this assessment, the human bioavailability of nickel was assumed to be 1 to 10% for ingestion, 13.6 to 19% for inhalation, and 0.06% for dermal exposures. Given that the sole source of nickel refining dust and nickel subsulfide is nickel refining operations (ATSDR, 1998), it is not possible that the nickel on site is in either of these forms; therefore, these limits were not used in the current assessment. Therefore, only the most conservative non-carcinogenic endpoints for nickel were considered for this assessment. The RfDs of 1.3 and 0.0012 µg Ni/kg body weight/day for nickel chloride and nickel sulfate, respectively, were adopted as the oral and inhalation exposure limits, respectively, for the current assessment of nickel toxicity.

4.5.4 References

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PART 4.6
TOXICOLOGICAL REVIEW: SILVER

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4.6.0 TOXICOLOGICAL REVIEW: SILVER

4.6.1 Fraction Absorbed *Via* Different Routes

4.6.1.1 Fraction Absorbed Via Ingestion

Ingestion of silver from food and water is the major route of exposure to humans (U.S. EPA, 1985). The ICRP (1960) reported that 1% of silver was absorbed by ingestion. From reviewing available animal studies, the U.S. EPA (1977) determined that approximately 10% of ingested silver is absorbed. Smith and Carson (1977) reported the amount of silver absorbed by ingestion to be low, while East *et al.* (1980) estimated the oral absorption of silver to be 18%. This value was based on a study of one woman with silver intoxication and was considered to be an over-estimate of bioavailability (East *et al.*, 1980; U.S. EPA, 1985; U.S. EPA, 1998). Furchner *et al.* (1968) calculated a gastrointestinal tract equilibrium absorption factor of 4.4% humans, which they considered to be a conservative estimate, as it was derived from absorption/retention studies with experimental animals. The value of 4.4% was rounded to 4% and used by the U.S. EPA to calculate an oral RfD (U.S. EPA, 1998). For the current exposure assessment, the 4% value, selected by U.S. EPA (1998), was used as the fraction of silver absorbed by ingestion.

4.6.1.2 Fraction Absorbed Via Inhalation

Air is a minor source of silver intake in comparison to food and water. Quantitative data regarding the amount of silver absorbed by inhalation is sparse (U.S. EPA, 1985). As a result, the fraction of silver absorbed by inhalation was not available in the literature. Based on airborne particle dynamics in the respiratory system, about 13% of airborne particulates would enter the lungs, and thus 13% of particulate-sorbed silver would be bioavailable in the lungs. Approximately 60% of airborne particles would be cleared by the mucociliary apparatus and swallowed. If 4% of the swallowed silver were absorbed from the gastrointestinal tract, then an additional 2.4% (4% of 60%) of airborne silver would be bioavailable by this route. Therefore, the total bioavailability of airborne silver from particles would be approximately 15.4% (13% from the respiratory system plus 2.4% of the cleared material).

4.6.1.3 Fraction Absorbed Via Dermal Exposure

Therapeutic use of silver has demonstrated that dermal absorption of silver occurs through broken skin and mucous membranes. However, it is not certain whether silver can infiltrate intact skin (U.S. EPA, 1985). The U.S. EPA (1985) examined some animal studies that showed absorption of silver through intact skin. Wahlberg (1965) estimated that less than 1% of topically applied silver nitrate was absorbed by the skin of 20 guinea pigs. Dequidt *et al.* (1974) found measurable amounts of silver in the spleen, liver, and kidneys of 8 shaved Wistar rats which had been bathed daily with silver for three months. The absorption was not quantified in this study however. For the current exposure assessment, the value of 1% (Wahlberg, 1965) was chosen as the fraction of silver absorbed through dermal exposure.

This value was selected because it was the only value available in the literature and it assumes that the dermal absorption in humans is similar to that of guinea pigs.

4.6.2 Health Hazard Assessment

4.6.2.1 Animal Studies

Subchronic and Chronic Studies

Recent studies with mice have found that silver compounds induce slight autoimmune responses. Johansson *et al.* (1997) subcutaneously injected SJL/N and A.SW mice (8 to 10 weeks old) with 2.5 mg/kg body weight/day silver nitrate diluted in sterile water as a 0.1 mL injection on the dorsum every third day for 4 weeks. Numbers of T and B cells as well as the expression of cell surface activation and proliferation markers were monitored by flow cytometry. Antibody levels were measured by immunofluorescence techniques. The administration of silver produced a slight activation and proliferation of T and B cells; no other significant effects on the immune system were observed. Previous experiments by these authors reported no autoimmune effects following silver administration. However, silver has been reported by other researchers to induce the production of autoantibodies to fibrillarin in SJL/J mice (Bigazzi, 1997).

In a series of experiments, Olcott (1947; 1948; 1950) observed argyria (a blue-grey discolouration which effects the eye, skin and internal organs of the eyes and internal organs) of rats administered varying concentrations of silver salts in their drinking water. In one of these studies (Olcott, 1950), 0.1% silver nitrate administered to rats in drinking water for 218 days (dose of 89 mg/kg body weight/day) resulted in a statistically significant increase in the incidence of ventricular hypertrophy. However, upon necropsy, advanced silver pigmentation was observed in a number of organs, but the ventricular hypertrophy could not be attributed to silver deposition. In another study, the severity of argyria of the eyes of rats was quantified using a rating of 1, 2, 3 or 4 (Olcott, 1947). The lowest score was assigned at a point when the eyes were only slightly grey. Each of the 159 treated animals received drinking water solutions with 1,000 mg/L part silver nitrate 1,000 mg/L or 1 part silver chloride. The number of controls were not specified, nor were the observation points at which the ratings were recorded. The authors reported that an average intake of 3.2 grams of silver over a period of 218 days resulted in a rating of 1 in a total of 98 rats. After an average of 373 days and a corresponding intake of 5.65 grams, 84 scores of 2 were obtained. A score of 3 was assigned after an average 447 days, or an intake of 6.8 grams, in 37 cases. Only 8 animals received scores of 4 after approximately 553 days and a total of 9.4 grams of silver. The very slight effect observed after an average of 218 days could be considered a NOAEL, as suggested by U.S. EPA (1985). The total dose of 3.2 grams corresponds to a daily dose of 41.7 mg/kg/ body weight/day, assuming an average rat body weight of 350 grams.

Genotoxicity/Carcinogenicity Studies

Silver nitrate and silver chloride were shown to be non-mutagenic in studies by Demerec *et al.* (1951) and Nishioka (1975); however, no further information was available for these studies (U.S. EPA, 1998).

Silver is considered to be noncarcinogenic in both laboratory animals and humans (U.S. EPA, 1985; Clement International Corporation, 1990). Two long-term studies in rats have been conducted; however, both used injection, either subcutaneous or intravenous, as the treatment route. In one, the majority of tumours produced were at the site of injection (Schmahl and Steinhoff, 1960). The other reported no increase in tumour incidence following monthly injections over a period of 10 months for a total of 75 mg of administered silver (Furst and Schlauder, 1977). The database on animal carcinogenicity for silver is presently inadequate for any conclusions to be made. The frequent use of silver as a therapeutic agent in humans has provided no indication that it possesses carcinogenic activity (U.S. EPA, 1985; Clement International Corporation, 1990; U.S. EPA, 1998). The U.S. EPA presently classifies silver as D; not classifiable as to human carcinogenicity.

4.6.2.2 Human Studies

Thirty healthy volunteers orally administered 50 mg of silver leaf (metallic silver) daily for 20 days displayed statistically significant reductions in serum phospholipids, triglycerides, cholesterol, and blood sugars compared to measurements of these parameters made prior to silver administration (Sharma *et al.,* 1997). Accompanying these changes were a slight decrease in total serum lipids, a rise in HDL concentrations, and a statistically significant decrease in the concentrations of several plasma enzymes. Total protein and albumin concentrations in blood were unchanged compared to pre-treatment values. The authors concluded that ingestion of up to 50 mg silver leaf per day is safe and that administration of silver in this form could have therapeutic benefit for conditions such as diabetes, obesity and atherosclerosis.

Silver compounds have been used in medicine for centuries. The primary effect that has been observed in humans exposed to silver *via* therapeutic treatments has been argyria (U.S. EPA, 1985). Argyria results from the deposition of silver in the dermis and from silver-induced production of melanin, and although permanent, is not associated with any adverse human health effects (U.S. EPA, 1998). Argyria , resulting from the use of silver arsphenamine in the treatment of syphilis, was commonly observed before antibiotics were developed, but is now a rare occurrence (U.S. EPA, 1998).

Gaul and Staud (1935) reported 70 cases of argyria following oral and intravenous administration of organic and colloidal silver medications to syphilis patients. Data from 10 male and two female patients who were intravenously administered silver arsphenamine 31 to 100 times over a 2- to 9-year period (total dose of 4 to 20 g silver) indicated that in the majority of patients, argyria developed only at higher doses. The authors concluded that a total accumulated intravenous dose of 8 g silver (as arsphenamine) may produce clinical

signs of argyria; however, as silver accumulates over a lifetime, some individuals may develop argyria at lower doses. The lowest dose at which argyria was observed in this study was 4 g silver arsphenamine which converts to a dose of 1 g of metallic silver (4 g silver arsphenamine x 0.23, the proportion of elemental silver in arsphenamine), which can be considered a LOAEL. As this study presented no information on patients who did not develop argyria, a NOAEL cannot be established.

Most of the cases investigated by Gaul and Staud (1935) involved exposure to organic forms of silver and as such, are of somewhat questionable relevance to the assessment of the impact of inorganic silver on humans. Two individual case studies in which humans were orally exposed to inorganic silver reported that argyria occurred following total oral doses of 6.4 and 6.5 grams of silver (Blumberg and Carey, 1934; East *et al.*, 1980). However, these case studies were based on clinical reports from single individuals and the actual dose of silver ingested can only be estimated.

In a cross-sectional investigation of 27 Caucasian males occupationally exposed to silver compounds (*versus* 27 matched controls), no cases of generalized argyria were observed (Pifer *et al.*, 1989). In addition, optometric and visual contrast sensitivity tests revealed that no significant difference occurred between the exposed and control group, although 29% of the exposed group had ocular silver deposition while none of the control group members had silver deposition. Although the exposed group had increased concentrations of silver in their blood, feces, and hair compared to the control group, there was no indication that this silver exposure adversely affected the health of the exposed workers. A NOAEL from this study was not reported.

The U.S. EPA (1985), in calculating an ADI for silver, used an average of the ADIs obtained from the three human studies of argyria reported by Gaul and Staud (1935), Blumberg and Carey (1934) and East *et al.* (1980). This value was reported to equal 182 µg/day, or 2.6 µg/kg body weight/day. However, the use of these data in deriving an ADI is questionable as the Gaul and Staud (1935) study was based on an intravenous route of administration of organic forms of silver, the studies by Blumberg and Carey (1934) and East *et al.* (1980) were based on only one case each, and a NOAEL could not be established in any of these studies.

4.6.3 Exposure Limit

The silver oral exposure limit used in this assessment is the oral reference dose (RfD) of 5 µg/kg body weight/day (U.S. EPA, 1998). The U.S. EPA derived this oral RfD based on data from the Gaul and Staud (1935) study. The study endpoint was the development of argyria in humans, a condition characterised by a permanent but medically benign bluish-gray discolouration of the skin. The intravenous dose of 1 g metallic silver reported by Gaul and Staud (1935) was converted to an oral dose of 14 µg/kg body weight/day by dividing by the oral bioavailability (4%), an adult body weight of 70 kg and apportioning the dose over a 70 year period. The oral dose of 14 µg/kg body weight/day was considered a LOAEL. An uncertainty factor of 3 was applied to account for minimal effects in a subpopulation which

has exhibited an increased propensity for the development of argyria. As the endpoint is a cosmetic rather than an adverse health effect, a larger uncertainty factor was deemed unnecessary, even though the experimental subjects may have had compromised health (all were syphilis patients), and the fact that there are inherent uncertainties in converting an intravenous to an oral dose (U.S. EPA, 1998).

Neither Health Canada nor U.S. EPA exposure limits were available for inhalation exposure to silver. The American Conference of Governmental Industrial Hygienists (ACGIH, 1998) recommended a time weight average (TWA) threshold limit value (TLV) of 0.1 mg/m^3 for occupational exposure to silver metal. Critical effects include local or generalized argyria of the skin, eyes, and mucous membranes in industrial workers (ACGIH, 1991). The TWA-TLV was amortized from an 8-hour workday, 5-day workweek, to an exposure limit of 0.8 µg/kg body weight/day, assuming a 70 kg person breathing 23 m^3/day (Curry *et al.*, 1993) is chronically exposed for 24 hours per day, 7 days per week [0.1 mg/m^3 · 23 m^3/day · 1/70 kg · 1000 µg/mg · 8 h/24 h · 5 days/7 days · 1/10 for non-cognisant exposure]. The safety factor of 10 was considered adequate because the oral RfD adjusted by the inhalation bioavailability is similar in magnitude (5 µg/kg body weight/day · 4%); also, the critical effect (argyria) is medically benign (U.S. EPA, 1998). The inhalation exposure limit of 0.8 µg/kg body weight/day for silver derived by CANTOX ENVIRONMENTAL Inc. from ACGIH (1998) was adopted for this assessment.

No data on dermal exposure limits for silver were identified in the literature reviewed for the current assessment.

For the purposes of this assessment, the bioavailability of silver was assumed to be 4% for ingestion, 15.4% for inhalation, and 1% for dermal exposures.

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CANTOX ENVIRONMENTAL

DELORO VILLAGE
EXPOSURE ASSESSMENT AND HEALTH RISK CHARACTERIZATION FOR ARSENIC AND OTHER METALS

PART 5 - HUMAN HEALTH RISK ASSESSMENT

December, 1999

PART 5
HUMAN HEALTH RISK ASSESSMENT - DELORO VILLAGE

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1.0 PROBLEM FORMULATION

Problem formulation acts as an information-gathering and interpretation stage, which is conducted to plan and focus the approach of the risk assessment on critical areas of concern for the site being evaluated. The key tasks requiring evaluation within the problem formulation phase included the following: i) site characterization, which consisted of a review of available site data to identify factors affecting the availability of contaminants to potential receptors, such as location and medium of contamination; ii) chemical characterization, which involved the identification of the primary chemicals of concern based on site monitoring; iii) receptor characterization to identify "receptors of concern", which included those with the greatest probability of exposure to chemicals from the site and those that have the greatest sensitivity to these chemicals; and, iv) the identification of exposure pathways, which took into account chemical-specific parameters, such as solubility and volatility, characteristics of the site, such as physical geography, geology, and hydrogeology, as well as the physiology and behaviour of the receptors.

1.1 Site Characterization

Several members of the CANTOX ENVIRONMENTAL team attended a site visit in Deloro on August 12, 1998, in order to determine characteristics of the village and the contamination relevant to the exposure and risk assessment.

As stated earlier, the area of concern in the current assessment is the village of Deloro, Ontario, and is adjacent to a former mine and refinery operation. The village is located along the perimeter of the mine site, with residences located immediately at the mine entrance. The village consists of 65 residences, many with sizable yards and home gardens. The area surrounding the village is rural, with both wooded areas and agricultural fields. The population of Deloro consists of 140 citizens, 40 of which are children. While the village is located on the Moira River, a survey of the population has indicated that the river in the immediate vicinity of the village is not used for swimming or fishing.

1.2 Chemical Selection

The screening level assessment conducted by the OMOE (1998), based on concentrations in surface soil, drinking water (1 sample) and vegetables (beets and lettuce), forms the basis for the selection of chemicals of concern in the current assessment. Elevated levels of arsenic had been determined on former mine site, with stockpiles specifically in the form of arsenate (As_2O_5, containing arsenic in its pentavalent form, As [V]). Based on comparisons to generic soil quality criteria of the OMOE and other jurisdictions, as well as estimations of daily intake of arsenic from various pathways, it was concluded that arsenic and, to a lesser extent, lead, nickel, cobalt, and silver, potentially posed an unacceptable risk to the residents of Deloro village.

Therefore, for the purposes of this assessment, the monitoring program of environmental media within Deloro village was expanded to include determination of arsenic, cobalt, lead, nickel, and silver in the following:

(i) indoor airborne particulates (low-volume samples);
(ii) indoor dust (swipe);
(iii) outdoor airborne particulates (high-volume samples);
(iv) outdoor dust (swipe samples and dust fall);
(v) well water; and
(v) samples of home grown produce.

These samples, together with the surface soil analysis, provided the data on which the exposure assessment of Deloro residents was based.

1.3 Receptor Selection

In the selection of receptors of concern, it is necessary to identify receptors that will be at the greatest potential risk from the site, either through having the greatest probability of exposure to chemicals from the site or through having the greatest sensitivity to these chemicals. In order to allow a comprehensive assessment of all possible receptors, both for the purpose of risk characterization and for use in the validation in comparison to the biological monitoring data, receptors from each of five age classes were selected:

- infant (0 to 6 months);
- preschool child (7 months to 4 years);
- child (5 years to 11 years);
- adolescent (12 to 19 years); and
- adult (20 years and over).

In addition, for the assessment of carcinogenic risk, that is, assessment of the incremental risk of cancer over a lifetime, a composite receptor was assessed, representing cumulative exposure over an entire lifetime which consists of each of the above age classes.

Parameters describing the physiological and behavioural characteristics of each receptor which were used in modelling of the magnitude of expected exposure are provided in Appendix A.

1.4 Exposure Characterization: Scenarios and Pathway Analyses

1.4.1 Exposure Pathways Analysis

Exposure pathways describe the routes through which contaminants in the environment (soil, air or water) come into contact with receptors of concern. These pathways may require direct contact between receptors and media of concern (*e.g.*, ingestion of soils), or may rely on indirect pathways which require movement of the chemical in the environment (*e.g.*, transfer of chemicals from soil into vegetables or meat and then to receptors through the foodchain).

Although behavioural and physical characteristic vary as a function of age class, all human receptors, regardless of age (with the exception of infants for specific pathways) would be subject to the same set of exposure pathways while within the town of Deloro. The following is a list of exposure pathways to which the residents of Deloro may potentially be subject, and which have therefore been evaluated in the current assessment:

(i) *Direct contact via soils:*
- Incidental ingestion of outdoor dust/soil;
- Incidental ingestion of indoor dust/soil;
- Dermal contact with soils/dusts while spending time outdoors;
- Dermal contact with indoor dust/soil;

(ii) *Direct contact via airborne particulates:*
- Inhalation of outdoor air-borne dusts;
- Inhalation of indoor air-born dust;

(iii) *Direct contact via water:*
- Consumption of municipal or well water;

(iv) *Indirect exposure via the food chain:*
- Consumption of home grown produce;
- Consumption of other food types ("general food basket": dairy, meats, prepared foods, *etc.*)

There were other potential pathways of exposure, based on the media of concern for the village, however, these were not considered to provide opportunity for significant exposure and were therefore not assessed. For example, while individuals might be exposed through bathing or showering to chemicals in municipal water, the levels of exposure through dermal contact and/or inhalation of aerosols would be negligible for the chemicals of concern in the current assessment.

While there was the possibility that the Moira River watershed, and thus biota within the river and lake, may be contaminated with arsenic or the other metals of concern *via* groundwater migration, the current assessment was focussed upon exposures incurred within the village of Deloro. As a survey of the population indicated that waters in the vicinity of

Deloro are not used for swimming or fishing, exposure pathways such as ingestion of fish and river water, as well as dermal exposure to river water, was not assessed.

1.4.2 Exposure Scenario Development

Exposure scenarios describe the situations in which receptors may be exposed to chemicals of concern, and emphasize selection of parameters which impact on the magnitude of potential exposure. Thus, the exposure scenario should describe factors such as access to specific media, physical activities, time spent in contact with contaminated media, *etc.* For the current assessment of Deloro residents, several exposure scenarios were considered alone and in combination with one another, based on the likelihood that certain activities (*e.g.*, use of wells, consumption of home-grown produce) would be applicable to some, but not all, residents. Additional scenarios were developed with consideration of the need to provide sufficient sensitivity for the comparison of residential arsenic exposure estimates to measured biological data (*i.e.,* urinary arsenic levels from the residents of Deloro).

In general, while all receptors may potentially be subject to the same exposure pathways and the same measured environmental concentrations, the magnitude of exposure of the individual *via* those pathways is dependent on behavioural/physical characteristics of the individual. For example, the amount of time a receptor spends within the town will affect the amount of time spent in contact with potentially contaminated soils. Thus this and similar parameters required definition in the exposure scenario, in relation to age, sex and/or other factors on which it may have depended. For example, an adult may work outside of Deloro and therefore not spend as much time at home as a preschool child.

The following is a brief overview of each exposure scenario evaluated in the current assessment. It is important to keep in mind that the exposure scenarios presented are by no means independent in nature, but rather were somewhat interactive in the risk assessment. Many of the scenarios were considered to potentially overlap one another and in several cases specific results of one exposure scenario were used within another.

All five receptor age classes were evaluated. Each of the pathways described above were assessed, modified by time spent in Deloro, or outside the village (*i.e.*, at a typical background Ontario site). For the purposes of the exposure assessment, the town of Deloro was theoretically divided into four areas or zones, encompassing the residential areas, where the majority of residences and sampling locations were situated.

Exposure Scenario 1: Resident of Deloro

The exposure scenario considered children, teenagers and adults (workers/students) to be away from Deloro due to either work or school (as detailed in Appendix A), and those receptors who do not leave the town of Deloro on a regular scheduled basis *(i.e.*, stay-at-home receptors). During this time in which residents are away from Deloro, it was assumed exposure to contaminants of concern were at typical Ontario background levels. For stay-at-home infants, preschool children and adults (*i.e.*, a stay-at-home mother or father, or a retired

person), these receptors were assumed to occasionally leave town for various reasons, such as grocery shopping, visiting, *etc.* (refer to Appendix A for receptor specific time periods). During the time in which these receptors were away from Deloro, it was assumed that exposure to chemicals of concern were based on typical Ontario background levels in various media.

While in Deloro, the amount of time spent indoors and outdoors during summer/winter months has been examined as a function of receptor age class (as detailed in Appendix A).

Several variations of this exposure scenario were examined with regards to the consumption of home garden produce and the use of well water versus municipal supply. Because some residents may use these resources while others do not, exposures were predicted with and without consideration of well water and home grown produce consumption. Background exposures from the consumption of a general food basket were also incorporated into all final exposure estimates.

Trespassers on the Former Mine Site

Although the former mine site adjacent to the town of Deloro is considered to be a restricted area, the potential for trespassing does exist. Therefore, a trespasser scenario was evaluated which assessed the exposures associated with the possibility that receptors (most likely older children and teenagers) may periodically spend some amount of time on the restricted mine site. In the absence of any site-specific data, the amount of time spent at the mine site area was assumed to be 2 hours/week. While on the mine site, receptors may potentially be exposure to concentrations of chemicals of concern in soil and dust. The potential exposure estimates incurred from the mine site have been incorporated into the above-mentioned scenarios as a possible source of exposure.

Exposure Scenario 2: Typical Ontario Resident (Background)

Using typical Ontario background concentrations in various environmental media (*i.e.*, soil, water, air, fruits and vegetables, and the general food basket), scenarios similar to those above were evaluated. This scenario would consist of receptors described by the same characteristics as were used in Scenario 1 (*i.e.*, the out-of-town worker and student, as well as the stay-at-home children and parents). This scenario was required not only to compare and contrast typical background exposures with those predicted for the residents of Deloro, but it also played a role in defining estimated exposure levels within the scenario for exposure of Deloro residents. As mentioned previously, segments of the background exposure assessment were required by the various scenarios which were used to estimate exposures to Deloro residents.

1.5 Conceptual Model

A conceptual model summarizing the various aspects of the proposed risk assessment, the pathways of exposure for receptors of concern, and the interrelationship of data obtained in the literature review portions of this study and in the exposure and risk modelling efforts, is detailed in Figures 5-1 through 5-3 [see end of Part 5].

2.0 EXPOSURE ASSESSMENT

2.1 Introduction

The following subsections describe the specific methodologies, assumptions and rationale used in characterizing potential exposures to chemicals of concern found in the various environmental media (*i.e.*, water, soil, dust, air, and vegetation) in the village of Deloro. Specifically, each environmental media data set is examined in detail, with respect to deterministic and probabilistic exposure assessment purposes. In addition to the general methodology used to derive human exposures (on a μg/kg body weight/day basis), the supporting rationale behind each exposure-related assumption used in the current assessment is presented.

2.2 Deterministic And Probabilistic Environmental Media Characterization

As noted previously, in the characterization of the exposures and risks associated with a contaminated site (such as Deloro Village), two analytical techniques are routinely used: deterministic and probabilistic (*i.e.*, stochastic) analyses. In probabilistic analysis, probability distributions (in the form of probability density function, or PDF) are assigned to the parameters used in the assessment (*i.e.*, exposure or risk parameters) and risk estimates are expressed as cumulative distribution functions (or CDFs). In a fully deterministic analysis, point estimates for parameters describing exposure and toxicity are incorporated. Because these point estimates are selected to maximize exposure and risk, the deterministic analysis can be considered to be a "worst-case" assessment. For the purposes of this assessment, deterministic analyses were used initially, to characterize the plausible maximum and typical mean exposures experienced by Deloro residents . In cases where elevated risks were indicated by this analysis, the probabilistic analysis was employed for exposure estimation in order to provide a more realistic indication of risk.

2.2.1 Deterministic Analyses

For a given range of applicable environmental data (*e.g.*, soil, water, air, *etc.*), the mean and 95th percentile of the cumulative distribution representing the data were used as the appropriate point estimate values to assess the potential risk associated with the typical mean and plausible maximum potential exposure scenarios, respectively. It should be noted that when determining the plausible maximum environmental concentrations (*i.e.*, the 95th percentile of a given data set) a normal distribution was assumed. Refer to Appendix B for typical mean and plausible maximum environmental data used in the current exposure assessment.

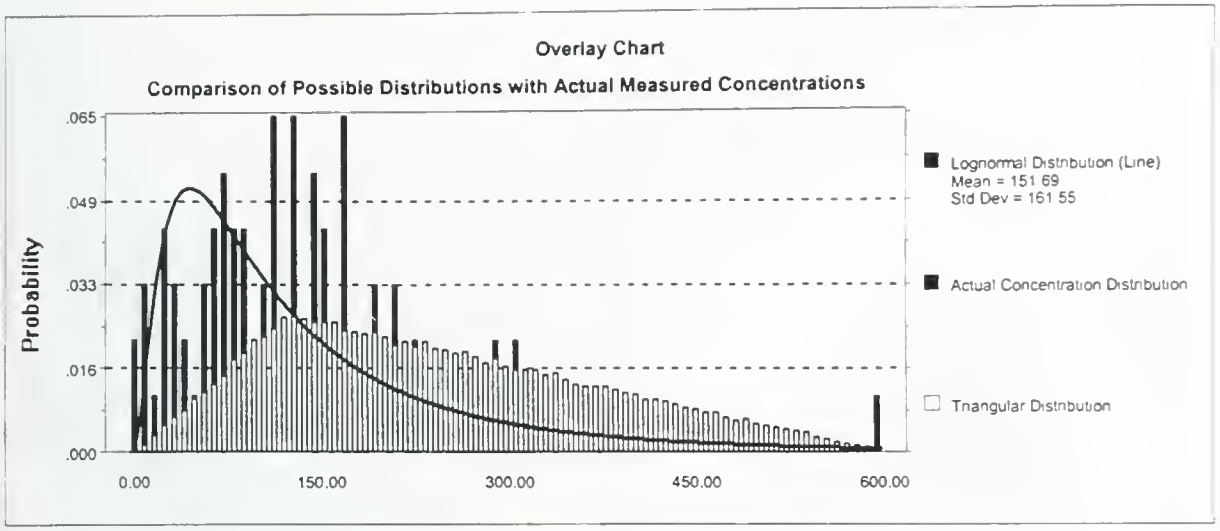
2.2.2 Probabilistic Analyses

An overview of the data indicated that a variable amount of sampling data is available for each of the respective environmental media (*e.g.*, soil, outdoor dust, well water, *etc.*). In such a case, care must be taken in establishing realistic and statistically valid continuous

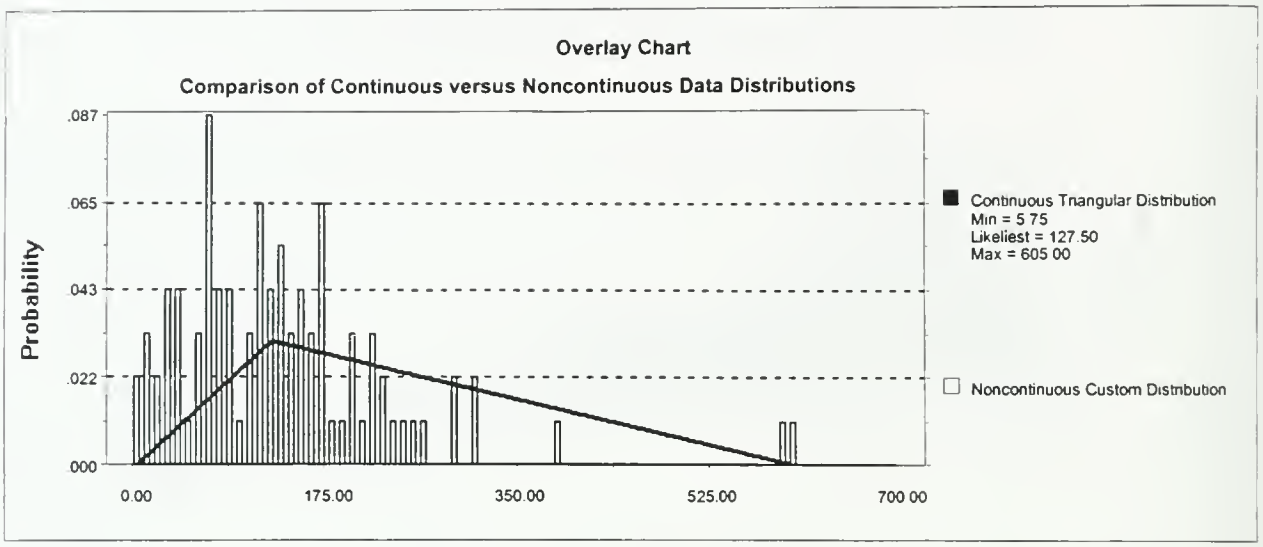
distributions to represent data collected for each of the various environmental parameters used in the exposure modelling exercises. Obviously, where distributions have to be assumed, technically rationalized judgement must be used, incorporating established scientific principles/practices for creating those distributions.

Initially, the statistical fitting package included as part of Crystal Ball® was used in an attempt to establish representative distributions to characterized environmental media concentrations in Deloro, using one of several standard goodness-of-fit statistical tests. Results of the fitting exercises indicated that there was insufficient data to attempt such distributional fitting in all but the soil concentrations from Zone 3, and the village as a whole. Both the Zone 3 soil data and the entire Deloro village soil data set indicated reasonable fits with several different distributional types, with the lognormal distribution appearing to be the most appropriate fit. However, an evaluation of the data using statistical tests related to the selection of probability distributions, suggested by the U.S. EPA (Singh *et al.*, 1997) and Burmaster and Hull (1996), indicated that both data sets "failed" the statistical tests for normality and lognormality. Given the inability of the data to conform to such a fitted distributional format, two other options for characterizing the individual data sets were considered.

The first option consisted of fitting each data set to a triangular distribution, corresponding to the minimum, median, and maximum values of the data. Given the limited amount of data available, the median, rather than the most-likely (*i.e.*, mode) value was used to represent the central pillar of the triangular distribution. This methodology had the advantage of retaining some of the shape of the overall distribution, while fitting a continuous distribution to the data (unlike a custom distribution). The result was a conservative distribution and was applicable to all the available data (*i.e.*, all zones and media), even under conditions of limited sampling data. The following overlay chart provides a comparison between a fitted lognormal distribution and a selected triangular distribution based upon the arsenic concentrations found in the soils of Zone 3. As demonstrated by the positioning of the actual concentration distribution, the triangular distribution would appear to provide a more adequate fit than the selected lognormal distribution. Furthermore, the triangular distribution was more conservative than its lognormal counterpart based upon the higher probability of sampling concentrations to the right of the mean/median values (*i.e.*, the triangular distribution was not skewed as heavily to the left as the lognormal distribution).



The second option involved using Crystal Ball® to fit a custom distribution to the full set of data by assigning a relative probability to each data point measured within a media or zone. This would provide a more accurate overall reflection of the distributional shape of each given data set and be less conservative than the triangular distribution option. However, as this method does not provide for a continuous distribution of the data, it would limit the usefulness of the probabilistic analysis when data is limited. Since this was the case for most media and zones for the current assessment, the probabilistic sampling would be restricted to only selecting values from within the limited set of measured data (these problems can be somewhat addressed by using the more computationally-intensive Latin Hypercube sampling methodology). Furthermore, based upon contaminant dispersal patterns, environmental concentrations of chemicals are typically continuous in nature, with considerable variation viewed even in areas of "hotspot" contamination. The following overlay chart provides a comparison between a continuous triangular distribution of the data with a noncontinuous custom distribution composed of the original arsenic soil sampling data set from Zone 3.



Analysis of the whole town soil concentration data indicated that several data points were statistical outliers. Outliers are extreme (high or low) values which are widely divergent from the main body of a group of data. Outliers were identified for whole town soil concentrations of arsenic and lead. A data point was deemed an outlier if the following conditions held:

data point value > UQ + o.c. * (UQ - LQ)

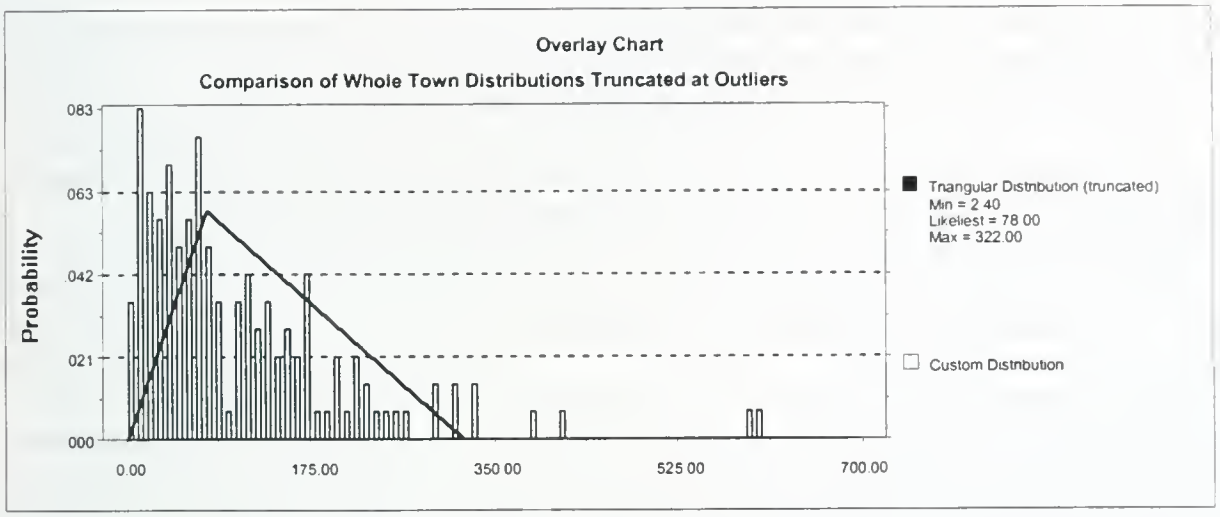
where:
UQ = upper quartile (75th percentile);
LQ = lower quartile (25th percentile); and
o.c. = outlier coefficient of 1.5.

Arsenic and lead concentrations above 321.6 and 383 mg/kg, respectively, were deemed outliers. See Table 5-1 for a summary of the chemical-specific parameters used for the determination of the outlier criteria.

Table 5-1 Parameters Used for Determination of Outlier Criteria.

Parameter	Arsenic	Lead
UQ	152.5	170
LQ	39.75	28

The following overlay chart provides a comparison between a continuous triangular distribution with outliers removed with a noncontinuous custom distribution composed of the original arsenic soil sampling data set from the whole town.



Given the limited amount of data available for most media and assessment zones, the more conservative methodology described within the first option (*i.e.*, establishing continuous triangular distributions to represent the data) was used for the current assessment. For the assessment of the whole town, the statistical outliers were removed prior to establishing the continuous triangular distributions to represent the data.

2.3 Outdoor Soil Concentrations

Soil concentrations gathered from 147 different sampling locations (found within and immediately surrounding the town of Deloro) were used to help derived exposure estimates from several direct (*i.e.*, incidental soil ingestion, dermal contact with soil) and indirect exposure pathways (*i.e.*, consumption of home grown produce). The use of outdoor soil concentrations to characterize such media as indoor surface dust and home grown produce have been discussed in detail in Sections 2.4 and 2.6, respectively. To estimate exposures experience by a typical Ontario receptor, typical Ontario soil concentrations (as detailed in Appendix B) were used.

Dermal contact with soil and incidental soil ingestion were two direct exposure pathways evaluated in the current assessment by which receptors were exposed to chemicals. To estimate exposures *via* dermal contact with soil, an estimated area of exposed skin during the summer and winter months were derived. When possible, age-specific (*i.e.*, infant, toddler, children, adolescent, and adult) whole body surface areas were used in combination with corresponding age-specific body part surface area percentages reported by Anderson (1985) (as detailed in Appendix A). During the summer months a receptor's head, upper extremities (including arms and hands) and legs were assumed to be available for dermal contact, while during the winter months a receptor's head and hands were considered available for contact with soil and dust. Anderson (1985), reported individual male and

female body parts as a percentage of the whole body surface area for each year of a receptor's pre-adult life. Therefore, male and female data were combined and mean body part percentages were derived for each combined age class. Using the estimated area available for dermal contact with soil during the winter and summer months in combination with a soil/dust adherence factor resulted in an estimate of the mass of contaminant adhered to the skin on a daily basis. Using this estimated mass and a chemical-specific dermal bioavailability (refer to Section 3), exposure estimates were determined.

Exposures from incidental soil ingestion were estimated using a similar approach. Soil/dust ingestion rates, body weights, time activity patterns and chemical-specific oral bioavailabilities were used to derive exposure levels.

2.4 Interior Surface Dust Concentrations

Indoor swipe samples used to monitor interior surface dust concentrations were taken from approximately 58 buildings within the town of Deloro. Two swipe samples were taken from each residence for a sample size of 116. These swipe samples were expressed in units of mass (µg of contaminant) per swab, and each swab covered an area of 100 cm^2. The concentrations of the vast majority of swipe samples were less than the reported detection limit. The following table illustrates the reported number of indoor swipe samples that were reported as having concentrations below detection.

Table 5-2 Summary of Concentrations in Indoor Swipe Samples

Chemical	Detection Limit (µg/100 cm^2)	Number Of Samples with Concentrations Below Detection	Percentage of Samples with Concentrations Above Detection
Arsenic	0.25	96	17%
Cobalt	0.75	111	4%
Lead	5	100	14%
Nickel	0.5	25	78%
Silver	0.75	115	1%

There were a series of limitations in directly using swipe samples in estimation of exposures *via* indoor dust. In order to use interior surface dust concentrations in an exposure assessment, concentrations must be expressed on a gravimetric basis (*i.e.*, weight of chemical/weight of dust basis), and some uncertainty would be inherently associated with converting this measured data to a usable form. The large number of samples with reported concentrations below the detection limit was considered to increase the uncertainty associated with this data set. Additionally, use of swipe samples in exposure assessment is in general considered to be uncertain, as exposures could be underestimated because dusts in crevices and/or associated with porous materials may not be sampled. Alternate methods would include vacuum sampling, although use of the vacuum is also associated with uncertainties and possible underestimation of exposure. Sampling of indoor dust by any method may be inadvertently hindered by the homeowner; additional cleaning in response to knowledge about a possible contamination problem and/or tidying prior to having "guests" (the sampling team) may result in artificially reduced indoor dust levels. Given these limitations, including

the number of samples below detection as well as uncertainties inherent in analysis of indoor dust, other means of estimating indoor dust concentrations were reviewed.

There are data in the published literature regarding the relationship between arsenic concentrations in outdoor soil (the primary source of indoor dusts) and concentrations in indoor dust. Because the outdoor soil sampling and analysis programme in Deloro was highly comprehensive in terms of number of samples and valid detection limits, estimation of indoor dust concentrations based on outdoor soil concentrations was considered to be more robust.

Therefore, rather than using these data directly in the current exposure assessment and possibly underestimating concentrations in indoor dust, swipe samples were used indirectly as a "reality check" when comparing the swipe sample methodology to the soil/dust ratio methodology described below.

Soil/Dust Ratio Methodology

Hwang *et al.* (1997) and Calabrese (unpublished, as reported in Walker and Griffin, 1998) have undertaken comprehensive studies which in part examine the relationship of interior surface dust levels to outdoor soil concentration. Both Hwang *et al.* (1997) and Calabrese (unpublished) sampled interior dust and outdoor soil concentrations using different methodologies from the same subset of 25 households in Anaconda, Montana. The reported average outdoor soil and interior dust concentrations were significantly different, 192 mg/kg and 75.14 mg/kg, respectively from the Hwang *et al.* study, versus 75 mg/kg and 29 mg/kg from the Calabrese study, respectively. However, the relationship between the average interior surface dust concentration and outdoor soil concentrations were very similar. The ratio of the average interior dust to outdoor soil concentrations were calculated to be 0.391 and 0.389 for the Hwang and Calabrese studies, respectively. It was concluded that using the most comprehensive environmental media sampled (*i.e.*, over 140 composite soil samples) within Deloro and the relationship as described above would not only result in the appropriate expression of interior dust levels for use in an exposure assessment, but would also inherently correlate soil and interior dust on a spatial basis.

Alternatively, swipe samples could be used to estimate indoor dust concentration. Two methods of converting swipe samples concentrations (expressed on a weight per unit area) to exposure estimates (on a µg/kg body weight/day) basis were used to validate the outdoor soil to interior surface dust relationship determined by the Hwang *et al.* (1997) and Calabrese studies.

(i) Swipe Sample Method I

The first method assumes that a preschool child (age 1 to 4 years) has a hand surface area of approximately 420 cm^2. A dust adherence factor of 0.5 mg/cm^2 was assumed, resulting a mass of dust (210 mg) adhering to a preschool child's hand (*i.e.*, 0.5 mg/cm^2 x 420 cm^2 = 210 mg). It should be noted that the adherence factor of 0.5 mg/cm^2 is within the range of the

1.75 to 10 g/m^2/day recommended by U.S. EPA (1992). Using the maximum reported swipe sample of 2.5 µg arsenic per 100 cm^2, 5.25 µg of arsenic was estimated to be present on the hands. Assuming a 16.8 kg preschool child ingests all of the dust present on their hands in a given day, the estimated exposure (adjusted for oral bioavailability) was determined to be 0.06 µg/kg body weight/day.

(ii) Swipe Sample Method II

The second method involves converting swipe samples to a gravimetric form. Assuming the average depth of interior surface dust is approximately 2 mm or 0.2 cm thick and having a density of 1.0 g/cm^3, swipe samples were converted from a mass per unit area value to a mass of contaminant per mass of dust estimate. Given a maximum swipe sample of 2.5 µg of arsenic per 100 cm^2, an estimated dust concentration of 0.125 µg of arsenic/g of dust was produced. Using an average soil/dust ingestion rate of 80 mg/day for a 16.8 kg preschool child and adjusting for an oral dust bioavailability value of 19%, an estimated mean exposure of 1.14e-04 µg/kg body weight/day was estimated.

The following table illustrates the results of both swipe sample methods and the modelled indoor dust ingestion exposure predictions using the soil/dust ratio method.

Table 5-3 Comparison of Results of Three Methods of Estimation of Exposure *via* Indoor Dust Ingestion

Chemical	Swipe Sample Method One Exposure Estimate (µg/kg bw/day)		Swipe Sample Method Two Exposure Estimate (µg/kg bw/day)		Modelled Indoor Dust Ingestion Predictions (µg/kg bw/day)	
	mean	max.	mean	max.	mean	max.
Arsenic	0.06	0.06	0.000114	0.000285	0.0135	0.0935

Method Two resulted in exposure estimates significantly lower than both Method One and the modelled exposures. However, exposure estimates from Method One are similar to modelled exposures, falling between the typical mean and plausible maximum. Given that outdoor soil densities can range from 1.35 to 1.9 g/cm^3 (U.S. EPA, 1997), the interior dust density of 1 g/cm^3 used in Method Two may be an overestimation and thereby result in underestimation of dust concentrations and related exposures. Therefore, given that the Soil/Dust Ratio used by Hwang *et al.* and Calabrese provided a conservative estimate of exposure *via* dermal contact with indoor dusts, this methodology was used in the current assessment.

Dermal contact and incidental dust ingestion were two potential exposure pathways by which receptors may accumulate exposure to chemically impacted interior surface dust. To estimate exposures *via* dermal contact with interior dust, an estimated area of exposed skin (as described in Section 2.0) during the summer and winter months were used in combination with a soil/dust adherence factor, resulting in a mass of contaminant adhered to the skin on a

daily basis. Using this estimated mass and a chemical specific dermal bioavailability (refer to Section 3), exposure estimates were determined. Exposures *via* incidental dust ingestion were estimated using a similar approach. Soil/dust ingestion rates, body weights, time activity patterns and chemical specific oral bioavailabilities were used to calculate exposure levels as was described in Section 2.3 of the general methodology.

2.5 Indoor/Outdoor Air Concentrations

The analysis of indoor air sampled by a low-vol sampler indicated concentrations below the detection limits for mass of contaminant per filter media in all households. Two samples were taken from each household and given the lack of detection, the average household concentration was assumed to be one-half the detection limit.

Since outdoor air data for Deloro residences were available, it was suggested that this data be used to estimate indoor air concentrations. A study by Roberts *et al.* (1974) indicates that indoor air concentrations are approximately 75% of outdoor air concentrations. On this basis, the outdoor air data were used to model indoor air, conservatively assuming that outdoor air concentrations were the same in both summer and winter. It was not expected that this assumption would have a significant impact on the overall exposure estimates, since this exposure pathway is considered negligible relative to other exposure pathways (refer to Figures 5-14, 5-15, 5-29, 5-30, and 5-31 for details). Calculations based on outdoor air concentrations, in combination with age specific inhalation rates, body weights, time activity patterns (*i.e.*, the amount of time spent indoors) and chemical specific bioavailabilities (refer to Appendix A and Section 3) were used to estimate exposures to contaminants from inhalation of indoor air on a µg/kg body weight/day basis.

2.6 Home Garden Produce

2.6.1 Concentrations in Fruits and Vegetables

Typical Ontario background contaminant concentrations in home grown vegetables were estimated using typical Ontario surface soil concentrations and vegetation biotransfer factors. Soil-to-plant transfer or biotransfer factors were based on measured values from a study by Baes *et al.* (1984) and represent the ratio between elemental concentrations in vegetation (dry weight) to elemental concentrations in the root zone of soil (dry weight). Soil-to-plant transfer coefficients used in the current background assessment are outlined in the following table. The biotransfer factors from Baes *et al.* (1984) were also used in estimation of concentrations of the metals in fruit, with the exception of arsenic. There were data available on the transfer of arsenic in orchard soils into apples (Aten *et al.*, 1980), and the biotransfer factor calculated from these data (0.00072) was used in estimation of arsenic concentrations in fruit.

Table 5-4 Soil-to-Plant Transfer Coefficients Used in the Typical Ontario Background Assessment

Chemical	Soil-to-Plant Transfer Coefficient (µg/g dry weight plant / µg/g dry weight soil)	Reference
Arsenic	0.04	Baes *et al.*, 1984
Cobalt	0.02	Baes *et al.*, 1984
Lead	0.045	Baes *et al.*, 1984
Nickel	0.06	Baes *et al.*, 1984
Silver	0.4	Baes *et al.*, 1984

A phytotoxicology investigation of Deloro village performed by the OMOE (1998) provided data on soil and vegetables (bean pods, lettuce, beet root, and carrot root) concentrations at 7 different garden test plots within and surrounding the village of Deloro. The range of concentrations in these test plots did not encompass the range of concentrations in surface soil throughout Deloro. The maximum arsenic soil concentration found within the 7 garden test plots was reported to be approximately 65 µg/g, as compared to a village mean soil concentration of 163 µg/g (and a maximum of 605 µg/g). Given the high Deloro village soil concentrations relative to those found within garden test plots, it was considered to be conservative to estimate the concentrations in vegetables grown in soils with higher concentrations and to use these values in the exposure assessment. This was accomplished by using site-specific biotransfer factors (based on the garden plot data, as described below) in combination with the range of soil concentrations across Deloro.

Site-specific root and vegetation biotransfer factors (BTFs) were calculated based on the data collected during the Phytotoxicology Investigation (Fleming and Kuja, 1998). Root crop BTFs were based on beet root and carrot data while leafy or "other" crop BTFs were derived from bean pod and lettuce data. BTFs were calculated as the ratio of concentrations in the vegetables versus that in the soil, for each of the 7 garden test plots. This procedure was completed for each plant type (*i.e.*, bean pods, lettuce, beet roots, and carrot roots) and each garden. The resulting biotransfer factor related dry weight vegetation concentrations to dry weight soil concentrations (*i.e.*, µg chemical/g dry weight plant/µg chemical/g dry weight soil). The equation below describes the calculations used to derive site-specific biotransfer factors.

$$BTF_{ss} = CONC_{Veg} / CONC_{Soil}$$

where:

BTF_{ss}	=	site-specific biotransfer factor (µg chemical/g dry weight plant/µg chemical/g dry weight soil)
$CONC_{Veg}$	=	mean vegetation concentration (dry weight basis)
$CONC_{Soil}$	=	corresponding mean soil concentration (dry weight basis)

Results of the Phytotoxicology Investigation OMOE (1998) were interpreted by OMOE as suggesting that arsenic in Deloro soil are not readily available to vegetation for a variety of potential reasons related to soil characteristics. Deloro-specific BTF factors were lower than those reported by Baes *et al.* (1984) for arsenic and cobalt, whereas lead and nickel had higher BTFs. In the site-specific monitoring, a number of plant concentrations were reported to be less than the detection limit or to be present at trace amounts. Given this and the inherent uncertainty associated with any one particular reported plant and/or soil concentration, mean garden concentrations were used in combination with mean corresponding plant data to derive an average site- and chemical-specific BTF values. Table 5-5 outlines the mean root and leafy or "other" crop site-specific BTF values used in the current assessment.

Table 5-5 Calculated Site-Specific Root and Leafy Crop Biotransfer Factors

Chemical	Mean Root Crop BTF Values (µg/g dry weight plant / µg/g dry weight soil)	Mean Leafy Crop BTF Values (µg/g dry weight plant / µg/g dry weight soil)
Arsenic	0.013	0.0159
Cobalt	0.0128	0.0135
Lead	0.0867	0.0353
Nickel	0.139	0.033
Silver[1]	0.4	0.4

[1] In the absence of site-specific data, literature values provided by Baes *et al.* 1984 were used for silver.

These mean BTF values were used in combination with measured soil data to calculate fruit and vegetable concentrations on a dry weight basis. As for concentrations in fruit for typical Ontario consumers, the concentrations of arsenic in fruit was estimated based on data on transfer of arsenic into apples (0.00072) from the published literature.

Since the consumption of fruits and vegetables is generally reported on a fresh or wet weight basis, dry weight vegetation estimates were transformed to fresh weight concentrations. Conversion factors for moisture contents for different fruits and vegetables were provided by the OMOE *via* personal communication. For the root and "other" vegetable categories used in exposure estimation, conversion factors of 0.1 and 0.04 were used, respectively. These values correspond to beet roots and lettuce harvested during August. Biotransfer factors derived for leafy vegetables were also used for fruits on a dry weight basis, however an average moisture content of 0.157 (provided by the MOE as individual moisture contents for different fruit types) was used.

In order to ensure that plant growth could actually be expected to occur at the soil and plant concentrations observed or predicted for Deloro, the predicted fruit and vegetable concentrations were validated against phytotoxicological data in the published literature. Generally, the literature would indicate that predicted plant concentrations were within the

ranges at which growth might be impaired, but at which overt or lethal toxicity would not likely be expected. Arsenic concentrations associated with 50% growth reduction were 0.17, 7.6 and 2.86 mg/kg in plant tissues (green bean, radish, and cabbage, respectively) (Lepp, 1981), while Adriano (1986) reported that concentrations of 2.1 to 8.2 mg/kg indicated leaves of fruit trees with "excessive" amounts of arsenic. In comparison, concentrations of arsenic in fruits and vegetables predicted for Deloro home gardens were 0.07 to 0.15 (mean) and 1.1 to 4.4 mg/kg (maximum). Therefore, while the mean concentrations were less than the concentrations associated with 50% growth reduction, at the maximum predicted tissue values, there may be some impact on crop yield or general plant health. There were no toxicity data with regard to plant tissue concentrations in fruits and vegetables for lead, however, a NOAEL of 500 µg/g soil has been reported for radish, carrots, and spinach, based on a lack of impact on crop yield and plant health (Lepp, 1981). In comparison, the maximum plausible soil concentration in Deloro was 344 mg/kg, and only a single data point (655 mg/kg) was greater than this NOAEL. With regard to cobalt, Kabata-Pendias and Pendias (1984) reported toxicity to bush beans at 1.72 to 5.68 mg/kg (wet weight). These values are much higher than the mean values predicted for fruits and vegetables in Deloro (up to 0.12 mg/kg), and higher than the maximum values as well (up to 1.29 mg/kg). Adriano (1986) reported that nickel concentrations in plant tissues of 50 mg/kg (dry weight) (correlating to 5 and 7.8 mg/kg wet weight for roots and fruit, respectively) were associated with general toxicity. The concentrations predicted for Deloro plants were 0.058 to 0.62 mg/kg (mean) and 0.25 to 9.05 mg/kg (maximum). Therefore, while the mean concentrations are not likely to be associated with overt toxicity, the maximum (for root vegetables) may be associated with overt toxicity and reduction in crop yields. There were little data available regarding toxicity of silver to plants, although Kabata-Pendias and Pendias (1984) reported toxicity at 2 mg/kg soil. In comparison, mean and maximum soil concentrations in Deloro were 3.73 and 9.75 mg/kg, respectively. Therefore, given that the phytotoxicity database is extremely limited, it would be expected that there might be some impairment of growth in vegetables grown at the mean and maximum concentrations. It must be noted that because the database likely considers only a single species, and that different species would have differing susceptibilities to toxic effects, the confidence in predicting toxic effects of silver in vegetables or fruits growing in Deloro is very low.

2.6.2 Estimation of Dietary Intake via Home Garden Produce

The typical mean total daily consumption rates for several categories of potentially home grown produce (total fruits and fruit juices; root vegetables; and other vegetables) were estimated to be approximately 527 g/day for children (268 g fruit/d, 259 g vegetables/d) and 570 g/day for adults (245 g fruit/d, 325 g vegetables/d) (Richardson, 1997). Refer to Appendix A for further details regarding receptor consumption patterns.

In the current assessment, home garden produce was considered to provide a potential pathway of exposure for Deloro residents. In order to assess the potential exposures of Deloro residents to contaminants in fruits and vegetables, it was necessary to determine the proportion of this intake which could be grown in a back yard garden. The dietary fruit and vegetable intakes of all Deloro residents, with the exception of the infant, were considered to

be potentially supplemented by home garden produce. The infant diet is expected to be comprised of breast milk or formula and pablum, with possible intakes of baby foods in the latter months of this age class. While the baby foods, consisting of juice and strained foods, could possibly be made from home gardens, it is expected that the majority of this would be bought in prepared forms. Therefore the infant was assumed to not consume any home garden produce.

The consumption of home-grown vegetables is limited by the crop yield and size of the garden, while the consumption of fruit is limited by yield and garden size as well as the types of fruits consumed. For example, a significant proportion of typical fruit intake consists of citrus fruits, which could not be grown in Deloro. Therefore, it was necessary to determine what proportion of the fruit consumption could be grown in a temperate climate, and to then determine what proportion of fruits and vegetables could be derived from a typical home garden. Based on the consumption data, the percentage of fruits and vegetables consumed by an individual belonging to a family of four which could be grown in a home garden was estimated as detailed below.

It was assumed that Deloro gardens were of the same size and crop yield as that recommended as a typical back yard garden by OMOE (1995). With an average crop yield of 1.4 kg/m^2, and an average garden size of 30 m^2, the typical home garden, growing both fruits and vegetables, would be expected to produce 42 kg of fruits and vegetables per year (OMOE, 1995).

In order to estimate the proportion of home grown produce which is fruit and that which is vegetables, it was first necessary to determine the proportion of fruit and fruit juice consumption which could be derived from a home garden in Ontario. The apparent per capita food consumption rates (Statistics Canada, 1991) indicated that the proportion of fruits consumed by typical Canadians (1988 to 1989) which could be grown in this region of Canada (apples, blueberries, cherries, plums, raspberries, and strawberries) was 37 percent of the total fruit consumption. Thus, a typical adult and child would consume fruit which could be grown in Canada at a rate of 90.65 and 99.16 g/d, respectively. All of the vegetables consumed by Deloro residents were assumed to be grown in Canada, and therefore, potentially in a home garden. Therefore, the total consumption of fruits and vegetables potentially grown in this region of Canada, and potentially in a home garden, would be 416.6 and 358 g/d, for adults and children, respectively (*i.e.*, 90.65 g/d + 325 g/d; 99.16 + 259 g/d, respectively). Thus, the total consumption of potentially home-grown fruits and vegetables for a typical family (2 adults, 2 children) would be 565 kg/year (*i.e.*, 416.6 g/d x 365 d/yr x 2 + 358 g/d x 365 d/yr x 2 = 565,000 g/year).

Assuming the proportions of fruits versus vegetables in a typical home garden would equal the proportions of potentially home-grown fruits and vegetables consumed, as calculated above, this would mean that 24.5% and 75.5% of home grown produce would be fruits and vegetables, respectively. Apportioning the back yard garden yield of 42 kg/year between fruits and vegetables would therefore indicate that 10.3 kg/year (or 24.5% of 42 kg/year) would be fruits, while 31.7 kg/year would be vegetables.

Using the estimated yields of a home garden of 10.3 and 31.7 kg/year for fruits and vegetables, respectively, the overall contribution of the home garden to fruit and vegetable consumption, respectively, can be calculated. Given a total fruit and fruit juices consumption, for a family of four, of 374.5 kg/year, and a total vegetable intake for a family of 4 of 426.32 kg/year, the proportion potentially obtained from a home garden would be 2.7% and 7.4% for fruits and vegetables, respectively. This incorporates the assumption that the total yield from the garden is consumed, *i.e.*, that there is no loss due to wildlife browsing or spoilage. It should be noted that this calculation would, due to its basis on the yield of a home garden, would not take into account the harvesting and consumption of wild fruits such as berries. However, berry consumption is highly seasonal and would comprise a small fraction of the overall fruit consumption, and thus a very small proportion of the total diet. Therefore, it was concluded that consumption of wild berries would contribute negligibly to total intake *via* home garden produce.

2.6.3 Estimation of Chemical Exposure via Home Garden Produce

Using the results of both of the above exercises, the daily exposure to the chemicals of concern *via* the consumption of home grown fruits and vegetables was determined for each of the receptors by using age specific body weights and consumption rates in combination with chemical specific oral bioavailabilities.

For arsenic, because only the intake of inorganic species are of toxicological concern, the total arsenic concentrations in fruits and vegetables were converted to estimations of the concentrations of inorganic arsenic only. This was done using data on the proportion of inorganic arsenic, relative to total arsenic, in fruits and vegetables, as reported in the scientific literature. It appears that there are two data sets from which this proportion could be derived, that of the Ontario Ministry of the Environment (OMOE, 1987; Weiler, 1987), and that of Pyles and Woolson (1982). While there is some variability in the data, in general, proportions of inorganic arsenic in vegetables are less than 10%. Weiler (1987) reported a range of 0 to 5% inorganic arsenic in vegetables, while Pyles and Woolson (1982) determined that arsenate (As[V]) contributed 2.5%, 10%, 8%, and 16% of the total arsenic in broccoli, potato, swiss chard, and lettuce, respectively. Data on the proportion of inorganic arsenic in fruits is somewhat limited. The OMOE (1997) reported that apple juice contained inorganic arsenic at a proportion of 73% of the total arsenic. Weiler (1987) (also OMOE data) was cited as indicating that fruit contained 10% inorganic arsenic. MOEE (1994a) reportedly used a percentage of 5% inorganic arsenic in both fruits and vegetables in their estimation of dietary intake for Ontario residents. Therefore, for the current assessment, a proportion of 10% inorganic arsenic was used for both fruits and vegetables, as this was considered a conservative representative of the available data.

2.7 Background Market Food Basket

The general food basket is a potentially significant source of background exposure to the chemicals of concern, through the consumption of foods purchased in groceries, markets and restaurants. Typical background dietary intakes for inorganic arsenic, cobalt, lead, nickel, and silver reported in the published literature were used to estimate the daily absorbed exposure (on a per body weight basis) to chemicals from the consumption of a market food basket (refer to Section 2.10 for background or typical Ontario exposure rates, including dietary intake rates).

Because the inorganic form of arsenic is the form of toxicological importance, dietary intakes of arsenic must be considered in terms of the inorganic forms only. The proportion of total arsenic in foodstuffs that is inorganic has been shown to vary widely with the specific food type; proportions as low as 0% inorganic arsenic have been reported in saltwater fish, and proportions as high as 75% have been reported in dairy products, beef and pork (Weiler, 1987; CEPA, 1993). The daily dietary intake of arsenic utilized in the current assessment has been reported in the literature in terms of inorganic arsenic. The proportion of inorganic arsenic in vegetables, as discussed above, tends to range between 0 and 16% (Pyles and Woolson, 1982; Weiler, 1987). Weiler (1987) also cited a proportion of inorganic arsenic in fruit of 10%. OMOE (1987) reported the amount of inorganic arsenic as a percentage of total arsenic for various foodstuffs; milk and dairy products averaged 26%, meat (100%), poultry (41%), saltwater fish (1%), freshwater fish (15%), shellfish (16%), rice (43%), cereals (49%), fruit (apple juice: 49%), and tea (26%). The proportions reported by OMOE (1987) were used by Yost *et al.* (1998) in deriving a daily intake estimate for inorganic arsenic (see below). In their estimate of daily intake of inorganic arsenic in the diet, CEPA (1993) assumed an average percentage of inorganic arsenic of 37% of the total arsenic (see below).

Utilizing age and sex-specific food consumption rate data for 112 food categories representative of the Canadian diet, Yost *et al.* (1998) took the percentage of inorganic arsenic in the foods analyzed by OMOE (1987) and multiplied by the corresponding food concentrations reported by Dabeka *et al.*, (1993) to estimate total Canadian dietary intake of inorganic arsenic for 3 age/sex classes: (children ages 1 to 4; women ages 20 to 39; men ages 20 to 39). Consumption data were provided by the Nutrition Canada Survey of Department of Health and Welfare, Canada (Yost *et al.*, 1998). The total daily dietary intake of inorganic arsenic for these 3 classes was 4.8, 8.1, and 12.7 µg/day, respectively (Yost *et al.*, 1998). The average daily intake for all classes combined was 8.3 µg/day. Based on their analysis of the OMOE (1987) data, the authors concluded that as much as 21 to 40% of total dietary arsenic is present as the soluble inorganic forms. This suggests that dietary intake of inorganic arsenic may be higher than previously believed (Yost *et al.*, 1998).

Dabeka *et al.* (1993) had previously estimated daily Canadian dietary intakes for total arsenic, averaged over 6 Canadian cities, to range from 14.9 µg/day (F and M children aged 1 to 4), 29.9 µg/day (F and M children aged 5 to 11), 31.7 and 40.9 µg/day (12 to 19 yr old F and M, respectively), 34.1 and 59.2 µg/day (20 to 39 yr old F and M, respectively), 52.8 and 43 µg/day (40 to 65 yr old F 2and M, respectively), and 25.8 and 35.7 µg/day (>65 yr old F and

M, respectively). The overall average estimated daily dietary intake for the entire Canadian population was 38.1 µg/day. An earlier estimate of daily arsenic intake from food was reported to range from 2.6 to 101 µg/day for total arsenic in adults, with an average intake of 16.7 µg/day (Dabeka *et al.*, 1987). However, this study was based on limited data and only estimated daily arsenic intake for male and female adults. The data from Dabeka *et al.* (1987) as well as 1980's or earlier data from other countries, was previously used to estimate the daily intake of inorganic arsenic from food (GCDWQ, 1996); a dietary EDI of approximately 10.5 µg/day was estimated. Despite the limitations of the data used to derive this estimate, it is in agreement with the average daily inorganic arsenic intake for all age classes recently estimated by Yost *et al.* (1998) to be 8.3 µg/day. The estimated chronic daily intake of 11 µg/day from a typical Ontario background diet (Fleming and Kuja, 1998) is also in close agreement with the estimates of Yost *et al.* (1998), and GCDWQ (1996).

CEPA (1993) used the food concentration data of Dabeka *et al.* (1987) together with food consumption patterns from Nutrition Canada (1977) to estimate daily intakes of inorganic arsenic, as follows:

- 0.04 to 2.4 µg/kg body weight/day (0 to 0.5 years)
- 0.05 to 2.0 µg/kg body weight/day (0.5 to 4.0 years)
- 0.03 to 1.9 µg/kg body weight/day (5 to 11 years)
- 0.02 to 1.2 µg/kg body weight/day (12 to19 years)
- 0.02 to 0.6 µg/kg body weight/day (20 to 70 years)

For the purpose of the current assessment infants, preschool children and children were assumed to have a mean daily dietary intake of inorganic arsenic of 4.8 µg/day. Adolescents and adults were assumed to have a mean inorganic arsenic intake of 8.1 and 12.7 µg/day, respectively. To derive an estimated daily absorbed dietary dose of inorganic arsenic, these reported dietary inorganic intake rates were divided by their respective assigned age class body weights and adjusted by a food-specific arsenic bioavailability of 90%. The plausible maximum and potential range (used within the stochastic assessment) of total daily dietary intake of inorganic arsenic used in the current assessment were derived from the data provided by Environment Canada (CEPA, 1993). Ranges of estimated daily intakes of inorganic arsenic by Canadians were reported on a µg/kg body weight/day basis for all 5 age classes. Data were adjusted by the food specific arsenic bioavailability to derive an estimated daily absorbed dose.

Cobalt, lead, nickel and silver were assessed in a similar fashion to arsenic. Refer to Section 2.10 for chemical-specific dietary intake rates for these chemicals.

2.8 Water Ingestion

When estimating background exposures to chemicals *via* drinking water, typical Ontario drinking water concentrations were used. When concentrations less than detection limits were reported, the detection limit was used as the plausible maximum water concentration, while half the detection limit represented the typical mean (refer to Appendix B for typical Ontario drinking water concentrations of the chemicals of concern).

Deloro municipal well water data were reported for two separate sampling dates. One data point for each chemical and sampling time were supplied, except for silver, for which the water had not been analysed. All of the concentration of chemicals were reported to be below the detection limit in April of 1998. All samples obtained in May of 1994 were either reported to contain all chemicals except arsenic at concentrations below the detection limit or less than a measurable trace amount.

In addition to the municipal water data, first draw and flush water samples were taken from a number of different wells within the village of Deloro. First draw samples were obtained from faucets following a prolonged period of non-use (*i.e.,* first faucet use in the morning), whereas flushed tap samples were obtained after running the water through the faucet for a short period of time (30 seconds or more). All flushed tap well water samples, except for lead (one sample) and silver (three samples) were reported to be below the limits of the method of detection used. First draw water samples for cobalt, nickel, silver, and arsenic showed no significant increase in overall water concentrations. A notable increase in first draw lead concentrations at some locations relative to corresponding flushed samples was observed; this may be indicative of lead-based plumbing (generally elevated first draw samples are due to leaching of elements from the faucet fixture during a period of non-use) at these locales. Only 2 of the first draw samples exceeded Ontario Drinking water objectives for lead, and while flushing the tap would decrease exposure, these concentrations are not indicative of chronic exposures, and therefore are not expected to be related to significant risks. Because the volume of first draw water is technically limited to the volume of the faucet (up to about 200 ml), this would represent a small proportion of the total water consumed per day. For the current assessment, first draw water samples were not considered a plausible long-term drinking water source and therefore were not considered in the current exposure assessment. Refer to Appendix B for the results of flushed, first draw and municipal water analyses.

As previously noted, all municipal water samples taken in 1998, except for silver (which had not been analysed) as well as the majority of flushed Deloro well water samples were below the reporting limit of detection. Detection limits used in the municipal water analysis were found to be different than those used for the on-site well water analysis, with a difference of more than 1 order of magnitude for lead and arsenic. Given that the majority of water samples taken (from both the municipal water and Deloro wells) were less than the reported detection limit, and that different limits were used in each analysis, a comparison of exposure estimates as a result of consuming well water versus municipal supply would only be a function of the detection limits used in each analysis. This was not considered a meaningful and/or relevant comparison and therefore both sets of data (municipal and well water were used together to estimate conservative concentrations in drinking water in Deloro)

In summary, 2 sets of data (one for Deloro and one for background) were used in the current assessment. The first set of data, as mentioned previously, was used to characterize typical Ontario exposures to various metals due to the consumption of drinking water. The second data set was used to characterize the exposure to metals present in Deloro drinking water and was developed from the municipal and Deloro well water data, presented in Appendix A.

Through the use of age-specific water intake rates, body weights, chemical specific oral bioavailabilities and water concentrations exposure estimates for each age class and scenario (*i.e.*, typical Ontario background and Deloro residents) were derived.

2.9 Exterior Surface Dust/Outdoor Dustfall/Indoor Dustfall

Exterior surface dust, outdoor dustfall and indoor dustfall samples were also collected as part of the analytical program. The exterior surface dust analysis was not provided on a gravimetric basis and was difficult to interpret. Concentrations appeared elevated for arsenic as compared to background, although not enough data were collected to allow for a statistical comparison. This data seemed to be consistent with data from other media (soil), and as a result this data was only used for comparative purposes. The majority of dust fall samples (>94%) were reported as less than the laboratory reporting limit for both indoor and outdoor samples. As a result, further interpretation of this data was not considered viable. The exposures associated with the pathways relevant to indoor and outdoor surface dust (*i.e.*, dermal contact and accidental ingestion) were assessed through the use of soil concentrations (Section 2.3) and estimated indoor surface dust concentrations (Section 2.4).

2.10 Data Used in Exposure Assessment for Typical Ontario Residents

As discussed earlier, the exposure assessment for typical Ontario residents, and the calculation of exposures of Deloro residents which occur outside of the village employed the same methodologies and calculations as have been described above. The concentrations considered representative of media throughout Ontario which were used in these calculations are presented in Table 5-6, below.

Table 5-6 Typical Ontario Soil, Air and Drinking Water Concentrations, and Dietary Intake for Typical Ontario Residents[1]

Chemical	Typical Ontario Concentration			Dietary Intake for Typical Ontario Residents (µg/person/day)
	Soil (mg/kg)[2]	Air (µg/m³)	Drinking Water (µg/L)	
arsenic	Ontario: 14 (agricultural) 17 (all other)	Ontario: mean 0.001, max 0.0019 (Dann., 1990)	Ontario DWSP[3]: <1.0 (MOEE, 1992)	Canadian: 4.8 (1 to 4 years) 8.1 (females:20 to 39 years) 12.7 (males:20 to39 years) (Yost *et al.*, 1998)
				Canadian: In µg/kg BW/day: 0.04 to 2.4 (0 to 0.5 years) 0.05 to 2.0 (0.5 to 4.0 years) 0.03 to 1.9 (5 to 11 years) 0.02 to 1.2 (12 to19 years) 0.02 to 0.6 (20 to 70 years) (CEPA, 1993)
cobalt	Ontario: 19 (agricultural land use)	<0.05 (Donaldson *et al.*, 1986)	0.1 to 5 (IARC, 1991)	1.7 to 100 (IARC, 1991)
	21 (all other land uses)		Canadian: <2 (Méranger *et al.*, 1979; 1981)	Canadian: 58 to 147 (mean = 102) (Méranger and Smith, 1972)
	Canadian: 5 to 50 (mean = 43) (McKeague and Wolynetz, 1980)			

Table 5-6 Typical Ontario Soil, Air and Drinking Water Concentrations, and Dietary Intake for Typical Ontario Residents[1]

Chemical	Typical Ontario Concentration			Dietary Intake for Typical Ontario Residents (µg/person/day)
	Soil (mg/kg)[2]	Air (µg/m³)	Drinking Water (µg/L)	
lead	Ontario: 55 (agricultural land use)	Canadian: <0.1 (Environment Canada, 1991)	Ontario range: <1 to 65; range of Ontario means: <1 to 4 (Graham, 1987)	Ontario:11.3 (0-6 mo) 17.7 (7 mo. to 4 years) 23.3 (5 to 11 years) 27.2 (12 to 19 years) 40.2 (20+ years) (MOEE, 1994b)
	120 (all other land uses)		range of Canadian means: 0.3 to <1.0 (Méranger *et al.*, 1979; 1981)	Canadian: 73 to 139 (mean = 106) (Méranger and Smith, 1972)
	Canadian: 5 to 50 (mean = 20) (McKeague and Wolynetz, 1980)		Ontario range: 1.1 to 30.7; median: 4.8 (Graham, 1988)[4]	Canadian: 22 to 150 (mean = 53.8) (Dabeka *et al.*, 1987)
	Toronto: 110 (average) (Roberts *et al.*, 1974)			Canadian: 138 (mean) (Kirkpatrick and Coffin, 1974)
				19.9 (mean for infants); 30.4 (mean for toddlers) (Gartrell *et al.*, 1986)
				Canadian: in µg/kg body weight/day: 1.1 (1-4 yrs old) 0.75 (adults) (Salminen, 1990);
				Canadian: 15 (avg - 2 yr old) 52.5 (avg - adult) (GCDWQ, 1996)
nickel	Ontario: 43 (all land uses);	Canadian cities: 0.001 to 0.026 (Dann, 1990; 1991)	range of Ontario means: 0.2 to 7.2 (Jenkins, 1992)	Canadian: In µg/kg BW/day: 22 (0-0.5 yr); 16 (0.5-4 yr); 10 (5-11 yr); 5.7 (12-19 yr); 4.4 (20-70 yr) (CEPA, 1994)
	Canadian: 5 to 50 (mean = 20) (McKeague and Wolynetz, 1980);		range of Canadian means: 0.6-2.0 (Méranger *et al.*, 1979; 1981)	
	Canadian: 1 to 67 (mean = 22) (McKeague *et al.*, 1979)			
silver	Ontario: 0.35 (agricultural);	<0.05 (WHO, 1984)	Ontario DWSP: <0.05 (MOEE, 1992)	Canadian: 7.1 (Gibson and Scythes, 1984)
	0.42 (all other land uses);			
	Canadian: <0.1 to 5 (mean = 0.1) (Boyle, 1968)			20 to 80 (WHO, 1984)

1 Shaded cells indicate the data selected for use in the current assessment
2 OMOEE, 1997 unless indicated otherwise.
3 DWSP: drinking water surveillance program data on raw drinking water from treatment facilities
4 Composite samples from 40 homes in Ontario at seven locations over a one-week sampling period (Graham, 1988) [considered the most realistic estimate of background drinking water lead intake]

3.0 TOXICOLOGICAL ASSESSMENT

3.1 Derivation of Toxicological criteria

Based on the principles discussed in Part 2, Section 3, the toxicity of each of the chemicals of concern was reviewed for the purposes of the current assessment. While, as per the requirements of the OMOE, all toxicological criteria used in this assessment were those recommended by regulatory agencies such as Health Canada, the U.S. EPA, and the OMOE, a comprehensive review of the critical toxicological literature was included (see Part 4). In this way, the evaluation of toxicity for each chemical, and specifically the risks associated with each, could be put into the perspective of the entire toxicological database. Development of toxicological criteria by these regulatory agencies included consideration of sensitive subgroups of the population, both through use of the most stringent scientifically-sound data, as well as application of uncertainty factors in the derivation of the criteria. This yields lower toxicological criteria which would be protective of the individuals most sensitive to the toxicity of the chemical, whether due to differences in genetics, life stage, nutrition, or health status.

Toxicological criteria selected for this assessment, the basis for the toxicological criterion, and the regulatory agency which adopted the limit, are summarized in Table 5-7. Toxicological criteria for chemicals considered to have threshold-type dose-responses are expressed as Reference Doses (RfD), while the limits for non-threshold-type dose responses are expressed as unit risk factors (q_1^*).

Table 5-7 Summary of Toxicological Criteria for Human Health Risk Assessment

Chemical	Route	Toxicological criterion		Endpoint	Study	Regulatory Agency
		Type	Value			
Arsenic (non-carcinogenic)	Oral	RfD	0.3 µg/kg bw/d	hyperpigmentation, keratosis, possible vascular complications (human)	Tseng *et al.*, 1968; Tseng, 1977	U.S. EPA, 1998
Arsenic (carcinogenic)	Oral	q_1^*	0.0015 (µg/kg bw/d)$^{-1}$	skin cancer, basal and squamous cell carcinoma (human)	Tseng *et al.*, 1968; Tseng, 1977	U.S. EPA, 1998
	Inhalation	q_1^*	0.013 (µg/kg bw/d)$^{-1}$	lung cancer (human)	Enterline and Marsh, 1982; Higgins, 1982; Brown and Chu, 1983a,b,c; Lee-Feldstein, 1983	U.S. EPA, 1998
Cobalt	Oral	RfD	60 µg/kg bw/d	polycythemia (human)	not specified	U.S. EPA, 1997
	Inhalation	RfD	0.01 µg/kg bw/d	metaplasia of larynx (rat/mouse)	Bucher *et al.*, 1990; NTP, 1991	ATSDR, 1997
Lead	Oral	RfD	1.85 µg/kg bw/d	subclinical neurobehavioural and developmental effects (child)	OMOE, 1994a	OMOE, 1996
	Inhalation	RfD	1.85 µg/kg bw/d	subclinical neurobehavioural and developmental effects (child)	OMOE, 1994a	OMOE, 1996
Nickel	Oral	RfD	1.3 µg/kg bw/d	increased mortality of litter (rat)	Smith *et al.*, 1993a	Health Canada, 1996
	Inhalation	RfD	0.0012 µg/kg bw/d	lung and nasal lesions (rat/mouse)	Dunnick *et al.*, 1989	Health Canada, 1996
Silver	Oral	RfD	5 µg/kg bw/d	argyria (human)	Gaul and Staud, 1935	U.S. EPA, 1998
	Inhalation	RfD	0.8 µg/kg bw/d	argyria of skin, eyes, and mucous membranes (human)	ACGIH, 1991	ACGIH, 1998

3.2 Summary of Bioavailability Values

As discussed in Part 2 of this report, bioavailability is an important consideration in the assessment of both exposure and toxicity. Therefore the literature was reviewed in order to identify bioavailabilities for each route of exposure, and where possible, values were selected to be specific to species (*i.e.,* humans) and to media of concern (*e.g.,* soil, water).

Bioavailability adjustment allows the estimation of internal doses, given specific bioavailability factors for specific routes of exposure. This adjustment is essential when comparing exposures to toxicological criteria of different exposure routes, and also allows use of study-specific bioavailabilities in the development of internal doses corresponding to the toxicological criteria. Briefly, both the exposure estimate and the toxicological criterion are adjusted for bioavailability, and the risk characterization is based on internal exposures and internal acceptable doses. In cases where both the exposure estimate and the toxicological criteria are subject to the same bioavailability factor, the bioavailability would in effect cancel out, as the same value is used for both the exposure and hazard assessments.

The U.S. EPA uses a default value for oral bioavailability of 80%, where data are lacking; however, in the selection of oral bioavailabilities for use in risk assessment, it is necessary to consider the scientific data regarding the impact of the chemical itself, the species in which the chemical is present, as well as the environmental matrix in which it is found.

The oral bioavailability of arsenic compounds is greatly dependent both on chemical species and on the matrix in which it is administered. As discussed in greater detail in Part 4.2, both clinical and laboratory studies indicate a absorption of greater than 95% of water-soluble inorganic trivalent arsenic following consumption of drinking water (*e.g.,* Pomroy *et al.*, 1980). Reduced oral bioavailability is observed with the less soluble forms of arsenic (arsenic trisulfide, lead arsenate, arsenic triselenide) in both humans and laboratory animals. There were no data in the published literature for the bioavailability of inorganic arsenic compounds in food. The OMOE (MOEE, 1994) cited an assumed value of 90% absorption of arsenic compounds in various food types; however, this value appears high given the information presented above on studies of various inorganic arsenic species.

The oral bioavailability of inorganic arsenic has been reported to be considerably reduced when administered in a soil or dust matrix. Oral bioavailabilities of arsenic, based on normalization for concentrations of arsenic in blood or urine following intravenous (i.v.) administration have been reported in the published scientific literature:

- 24% in rabbits in a soil matrix (normalized via urine) (Freeman *et al.*, 1993);
- 19 and 14% (normalized via urine) or 10 and 11% (normalized via blood) in female Cynomolgus monkeys, for arsenic in house dust and soil matrices, respectively, taken from the vicinity of a mine and smelter facility; and
- 8.3% in dogs, in a bog ore-containing soil matrix (normalized via urine) Groen *et al.* (1994).

The basis for the reduction of bioavailability of arsenic compounds in soils and house dusts in the vicinity of mining and smelter operations is related to the fact that arsenic from these sources tend to be in less soluble forms (*e.g.*, metal-arsenic oxides and phosphates) and, as a result of containment within a solid matrix, to be less accessible for dissolution or uptake (Davis *et al.*, 1996). This basis is supported by the environmental data available for Deloro, as the analysis of concentrations of arsenic in vegetation in Deloro indicated the fact that the uptake of arsenic into plants, which was studied within Deloro, would indicate that the arsenic tends to be less bioavailable than might be expected. This means that the specific form of arsenic in the soil is less likely to be taken up through root uptake as well as through biological mechanisms in mammals (*e.g.*, absorption in the gut).

Bioavailability values selected for this assessment are summarized in Table 5-8.

Table 5-8 Summary of Bioavailability Values for Human Health Risk Assessment

Chemical	Bioavailability (%)					
	Oral	Reference	Inhalation	Reference	Dermal	Reference
Arsenic	95% 90% 14% 19%	in drinking water: Pomroy *et al.*, 1980 in food: OMOE, 1994b in soil: Freeman *et al.*, 1995 in dust: Freeman *et al.*, 1995	30-34	Holland *et al.*, 1959	0.8-1.9	Wester *et al.*, 1993
Cobalt	18-97	Harp and Scoular, 1952; Sorbie *et al.*, 1971; Valberg *et al.*, 1969	24-71	APD[a]	0.06	Assumed[b]
Lead (adult)	3608 2	Kehoe, 1961; Thompson, 1971; Karhausen, 1973; Blake, 1976; Chamberlain *et al.*, 1978	19-22	APD[a]	0.06	Moore *et al.*, 1980
Lead (child)	42-53	Karhausen, 1973; Alexander, 1974; Ziegler *et al.*, 1978; Mushak, 1991	38.2-44.8	APD[a]	0.06	Moore *et al.*, 1980
Nickel	3580 4	U.S. EPA, 1986; ATSDR, 1992; Nielsen *et al.*, 1993	13.6-19	APD[a]	0.06	Assumed[b]
Silver	4	Furchner *et al.*, 1968; U.S. EPA, 1998	15.4	APD[a]	1	Wahlberg, 1965

a Airborne Particle Dynamics.
b Assumed to be the same dermal bioavailability as lead due to lack of data.

4.0 RESULTS AND DISCUSSION

As was discussed in detail in Part 2, risk characterization, the final step in risk assessment, consists of a comparison of estimated exposures to an acceptable level of risk or exposure. For non-carcinogenic chemicals the acceptable level is the toxicological criteria, and the comparison may be expressed as an Exposure Ratio [ER]. For carcinogenic chemicals, risks are expressed as Cancer Risk Levels (CRLs), and a comparison is made to acceptable levels of incremental cancer risk. Negligible cancer risk levels are generally considered to be $1x10^{-4}$ to $1x10^{-6}$, but evaluation of predicted cancer risks for a population must also consider predicted risks for a background or "typical" population, since "typical" populations are considered to be without undue cancer risks, predicted CRLs for these receptors can provide a valid "acceptable level" of risk. In cases where the estimated exposures or risks are less than the acceptable level, it can be concluded that there would be no risk of adverse health effects. When estimated exposures or risks exceed the acceptable level, consideration must be given to the possibility of adverse health effects, but such exceedences are not necessarily indicative of potential risks, but may reflect overestimation of risk due to the use of overly conservative estimates (*e.g.,* overestimating exposures through use of maximum soil ingestion rates). When evaluating risks, deterministic analyses were used initially, to characterize the plausible maximum ("worst-case") and typical mean exposures experienced by Deloro residents. In cases where the potential for measurable risks were indicated by comparison to the criteria and to risks of typical Ontario residents, it was concluded that a more rigorous and realistic evaluation of risks should be conducted through probabilistic analysis. The various uncertainties associated with each phase of the risk assessment were examined in order to ensure that the risk characterization would be both conservative and realistic. In all cases, the discussion and analysis of results focussed on the most sensitive receptor (composite for carcinogens and, infant or preschool child for non-carcinogens).

4.1 Deterministic Analysis

The deterministic analysis indicated that for non-carcinogenic endpoints, the infant and/or the preschool child were generally the most sensitive receptors of all the age-classes; based on carcinogenicity endpoint, the most sensitive receptor for arsenic was the composite receptor (representing cumulative exposure throughout a lifetime). The results of the deterministic risk characterization for background, the whole town, and for each of the geographical zones within Deloro are presented graphically for the preschool child (non-carcinogens) and composite receptor (carcinogens).

The results of these analyses are discussed below in terms of the implications for the potential occurrence of adverse health effects, the role of exposures through consumption of home garden produce and trespassing onto the mine site in relation to overall risks, and the comparison of the predicted exposures to the toxicological criterion, or consideration of the predicted cancer risk level (CRL) and/or risks predicted for typical Ontario residents, with regard to the necessity of progressing to a stochastic assessment. The comparison of predicted risks of Deloro residents to those of typical Ontario residents is important, because while the assessments are designed to provide a conservative estimation of risk, conservatism

may lead to a significant over-estimation of risk. Typical Ontario residents, as evaluated in the current assessment, are exposed only to background or ambient media concentrations (not influenced by point sources) of the contaminants of concern, and the calculations of exposure and risk are the same as those for Deloro residents. Thus the risk estimates for Deloro residents and typical Ontario residents would be similarly conservative, and a comparison of these values would provide a mechanism for determining if risk estimates for Deloro residents are actually elevated and indicative of increased risk of adverse health effects.

As stated previously, this assessment addressed risks based on concentrations representative of the town as a whole, as well as four geographical zones with the town.

4.1.1 Arsenic (Carcinogenic)

The composite receptor, indicating cumulative risks experiences over a lifetime, was the most sensitive receptor, which would be expected based on the definition of this receptor (*i.e.*, consisting of the addition of incremental cancer risks for each of the age classes). As the oral and dermal cancer slope factor was based on skin cancer incidence, while the inhalation slope factor was based on lung cancer incidence, the exposures and risks will be discussed in terms of risks for these specific cancer types.

The results of the risk characterization for the composite receptor are summarized in Tables 5-9 and 5-10, below, and Figures 5-4 and 5-5. The increments in total estimated cancer risks, comparing CRLs for typical Ontario residents, Deloro residents without consumption of home garden produce, with home garden produce, and with trespassing on the former mine site, are presented in Figure 5-6.

Table 5-9 Deterministic Arsenic Estimated Lifetime Cancer Risk Levels (ALL CANCERS)

	ESTIMATED CANCER RISK LEVEL			
	Home Garden Consumption		No Home Garden Consumption	
	plausible maximum	typical average	plausible maximum	typical average
TYPICAL ONTARIO RESIDENT				
TYPICAL ONTARIO	1.42e-03	2.56e-04	1.41e-03	2.53e-04
DELORO ALONE				
WHOLE TOWN	4.09e-04	1.14e-04	3.83e-04	1.07e-04
ZONE 1	1.42e-04	8.37e-05	1.39e-04	8.20e-05
ZONE 2	1.75e-04	9.08e-05	1.70e-04	8.79e-05
ZONE 3	3.97e-04	1.25e-04	3.77e-04	1.18e-04
ZONE 4	4.89e-04	1.51e-04	4.65e-04	1.38e-04
DELORO INCLUDING BACKGROUND				
WHOLE TOWN	1.71e-03	3.51e-04	1.68e-03	3.44e-04
ZONE 1	1.44e-03	3.21e-04	1.44e-03	3.19e-04
ZONE 2	1.47e-03	3.28e-04	1.47e-03	3.25e-04
ZONE 3	1.69e-03	3.62e-04	1.67e-03	3.53e-04
ZONE 4	1.79e-03	3.89e-04	1.76e-03	3.75e-04

Table 5-10 Deterministic Incremental Arsenic Estimated Lifetime Cancer Risk Levels (by cancer type) for Whole Town

	ESTIMATED CANCER RISK LEVEL	
	plausible maximum	typical average
ALL CANCERS COMBINED		
Typical Ontario resident	1.42e-03	2.56e-04
Deloro alone (no home garden consumption)	3.83e-04	1.07e-04
Deloro alone (home garden consumption included)	4.09e-04	1.14e-04
Deloro including home garden consumption & background contribution	1.71e-03	3.51e-04
LUNG CANCERS		
Typical Ontario resident	2.81e-05	2.75e-06
Deloro alone (no home garden consumption)	4.38e-07	1.75e-07
Deloro alone (home garden consumption included)	4.38e-07	1.75e-07
Deloro including home garden consumption & background contribution	3.94e-06	1.17e-06
SKIN CANCERS		
Typical Ontario resident	1.39e-03	2.53e-04
Deloro alone (no home garden consumption)	3.83e-04	1.07e-04
Deloro alone (home garden consumption included)	4.08e-04	1.14e-04
Deloro including home garden consumption & background contribution	1.70e-03	3.50e-04

As is indicated by these results, the predicted total cancer risk levels for the residents of Deloro, with and without consumption of home garden produce, were slightly higher than those predicted for typical Ontario residents. In evaluation of specific cancer types, it was apparent that the CRLs for lung cancer were significantly lower than that for skin cancer, indicating that the majority of the total estimated cancer risk is due to risk of skin cancer. In addition, as indicated by the results provided in Table 5-10, the predicted CRLs for lung cancer for Deloro residents were lower than those for Ontario residents, further supporting the conclusion that risks associated with exposure to Deloro-specific media were primarily, if not entirely, due to risk of skin cancer.

An examination of the contribution of various exposure pathways to the overall risks associated with environmental media in Deloro and from background sources indicated that more than 90% of the background risks were associated with general food basket for all receptors. In turn, background exposures contributed approximately 65 to 75% of overall

risks of Deloro residents (composite receptors) consuming home garden produce, and about 66 to 76% of overall risks of Deloro residents not consuming home garden produce.

Other contributors to the overall risks predicted for Deloro residents (home garden consumers, composite receptors) included drinking water from Deloro municipal supplies (about 20% of mean overall risks, and 5% of maximum risks) and soil/dust exposures (indoor and outdoor, dermal and oral), which contributed about 10% of mean risks and approximately 17% of maximum risks for the composite receptor. Home garden produce consumption contributed only up to 2% of mean and maximum risks.

The identification of general food basket, drinking water and dermal/oral exposures to soil and dust as major contributors to the estimated cancer risks associated with arsenic indicates that the majority of the risk (greater than 99.95%) of the risk is associated with oral and dermal exposures, and therefore a majority of the cancer risk is specifically risks associated with skin cancer, as indicated by the breakdown of cancer types in Table 5-10.

Because skin cancer risk estimates for residents of Deloro exceeded those predicted for typical Ontario residents, a probabilistic analysis was conducted based on the carcinogenic effects of arsenic.

4.1.2 Arsenic (Non-Carcinogenic)

The characterization of potential risks associated with exposure to arsenic, based on non-carcinogenic endpoints (*i.e.*, adverse effects on the skin, *e.g.*, hyperpigmentation, keratosis), indicated that the infant was the most sensitive receptor. The results of the assessment of arsenic on a non-carcinogenic basis, for the preschool child, are provided in Tables 5-11 and 5-12 and Figures 5-7 and 5-8.

Table 5-11 Deterministic Arsenic (non-cancer) Long-Term Exposure Ratio Values (preschool child) for Home Garden Consumers

	EXPOSURE RATIO VALUES			
	Home Garden Consumption		No Home Garden Consumption	
	plausible maximum	typical average	plausible maximum	typical average
TYPICAL ONTARIO RESIDENT				
TYPICAL ONTARIO	6.97	1.02	6.76	1.01
DELORO ALONE				
WHOLE TOWN	3.63	0.639	3.4	0.608
ZONE 1	1.29	0.44	1.26	0.433
ZONE 2	1.58	0.487	1.54	0.474
ZONE 3	3.53	0.707	3.35	0.668
ZONE 4	4.36	0.884	4.13	0.826
DELORO INCLUDING BACKGROUND				
WHOLE TOWN	10	1.57	9.77	1.54
ZONE 1	7.66	1.37	7.63	1.36
ZONE 2	7.96	1.41	7.91	1.4
ZONE 3	9.9	1.64	9.72	1.6
ZONE 4	10.7	1.81	10.5	1.75

Table 5-12 Deterministic Incremental Arsenic (non-cancer) Long-Term Exposure Ratio Values (preschool child) for Whole Town

	EXPOSURE RATIO VALUES	
	plausible maximum	typical average
Typical Ontario resident	6.97	1.02
Deloro alone (no home garden consumption)	3.4	0.608
Deloro alone (home garden consumption included)	3.63	0.64
Deloro including home garden consumption & background contribution	10	1.57

The maximum exposure estimates for Deloro (whole town and each zone) and typical Ontarians exceeded the toxicological criterion, as is indicated by an ER greater than 1.0, with and without consumption of home garden produce. Mean exposure estimates for infants and preschool children, for Deloro (with and without consumption of home garden produce) and

typical Ontarians, and for infants, preschool children, children, and adolescents in Zone 4 (with consumption of home garden produce), also exceeded the toxicological criterion. Mean exposures for all other receptors were less than the limit. In addition, risks predicted for Deloro residents were higher than those predicted for typical Ontario residents.

The major contributors to background and overall risks for Deloro residents are the same as that indicated for arsenic on a carcinogenic basis (Section 4.1.1). The majority of the risks associated with background can be attributed to general food basket, which contributes 55 to 65% of the overall risks predicted for Deloro residents (preschool children and adults) not consuming home garden produce, and about 60 to 75% of overall risks for receptors consuming home garden produce. Other exposure pathways contributing to risk included consumption of municipal drinking water in Deloro, dermal contact with soils and dusts (adults and children), soil/dust ingestion (children), and consumption of home garden produce. Contribution to exposure through dermal and oral exposures to soils and dusts were variable for the different age classes, dependent on receptor behaviour patterns. For example, soil/dust ingestion contributed around 10% of the risks predicted for infants and children, but less than 3% of that for adults. Dermal contact with soils/dusts yielded proportional contributions to maximum ERs of about 17% for infants and preschool children, and of more than 25% for adults. Contributions of this pathway to the mean ER estimates were about 7% for both small children and adults.

The exceedence of the toxicological criterion for arsenic, which was based on the induction of a specific skin condition in populations endemically exposed to high levels of arsenic in drinking water, was considered to be indicative of the need for a more rigorous examination of risks through probabilistic analysis. The results of the deterministic assessment were not considered indicative of definitive concerns regarding induction of adverse skin effects, for several reasons. The risks predicted for Deloro residents were slightly higher than those for typical Ontario residents. It is also important to note that the toxicological criterion for the skin condition associated with arsenic is reflective of long-term exposure to arsenic, and that even the mildest symptoms of the skin condition have not been observed in children less than 11 years of age (U.S. EPA, 1998). Thus, the lower risks indicated for teenagers and adults are more reflective of the actual risk of induction of keratosis and hyperpigmentation than are the risks predicted for young children. Because exposure estimates for children exceeded the toxicological criterion, and because risk estimates for induction of adverse skin effects in residents of Deloro exceeded those predicted for typical Ontario residents, arsenic was retained for stochastic analysis based on non-carcinogenic endpoints.

4.1.3 Cobalt

The risk characterization for cobalt, based on the most sensitive toxicity endpoints of polycythemia and metaplasia of the larynx, indicated that the most sensitive receptor for typical Ontario risks was the preschool child, while the infant was the most sensitive in terms of risks associated with exposures within Deloro. In terms of overall risk to residents of Deloro, the ERs indicated that the preschool child was the most sensitive at maximum exposures, while the child (aged 5 to 11 years) was the most sensitive for mean exposures.

The results of the risk characterization for cobalt for the preschool child are provided in Table 5-13, below, and Figures 5-9 and 5-10.

Table 5-13 Deterministic Incremental Cobalt Long-Term Exposure Ratio Values (preschool child) for Whole Town

	EXPOSURE RATIO VALUES	
	plausible maximum	typical average
Typical Ontario resident	3.51	1.2
Deloro alone (no home garden consumption)	0.0296	0.00951
Deloro alone (home garden consumption included)	0.0399	0.011
Deloro including home garden consumption & background contribution	0.681	0.252

Both the mean and maximum plausible estimates of exposure for residents of Deloro (whole town, and for each zone) were less than the toxicological criterion (as indicated by ERs less than 1.0), which indicates that there would be no measurable risk of adverse health effects (polycythemia or metaplasia of the larynx). Mean exposures for typical Ontario residents, however, approached, and for the preschool child, slightly exceeded, the toxicological criterion. The maximum typical Ontario exposures were slightly in exceedence of the toxicological criterion (up to about 3.5-fold for the preschool child). Thus, the exposure estimates for the whole town and for each of the zones within Deloro were less than the toxicological criterion, and risk estimates for Deloro residents were well below that for typical Ontarians, with and without the consumption of home garden produce.

Examining the major factors responsible for risks to typical Ontario residents associated with cobalt indicated that the majority of the risks were derived from inhalation exposure to outdoor and indoor air (contributing about 60 to 75% of the background risk). The typical Ontario air concentrations were, in turn, based on data in the published literature which indicated that ambient air concentrations of cobalt were less than a detection limit of 0.05 $\mu g/m^3$ (see Appendix B). Current monitoring efforts at Deloro had much lower detection limits, thereby providing much lower estimates of inhalation exposure. Thus the differences in background versus Deloro risk estimates were primarily due to the use of values based on the much higher detection limit for modelling of background exposures. Aside from the risks associated with inhalation, oral exposure *via* the general food basket consumption was responsible for the remainder of background exposures to cobalt.

Even with home garden produce consumption, exposures to cobalt from environmental media within Deloro contributed to less than 20% of the overall exposure and risk.

Therefore, based on both the comparison to predicted risks for typical Ontario residents and the comparison to the toxicological criterion, it was concluded that the exposures to cobalt

associated with environmental media in Deloro would not be associated with measurable risks of adverse health effects.

4.1.4 Lead

The risk characterization for lead, based on the toxic endpoint of impacts on neurobehavioural development, indicated that without home garden produce consumption, the infant was the most sensitive receptor for lead; with home garden produce consumption, however, the preschool child was the most sensitive receptor. The exposure ratios (ERs) for lead for the preschool child are presented in Tables 5-14 and 5-15 and in Figures 5-11 and 5-12. The increments in total risks, comparing ER for typical Ontario residents, Deloro residents without consumption of home garden produce, with home garden produce, and with trespassing on the former mine site, are presented in Figure 5-13.

Table 5-14 Deterministic Lead Long-Term Exposure Ratio Values (preschool child) for Home Garden Consumers

	EXPOSURE RATIO VALUES			
	Home Garden Consumption		No Home Garden Consumption	
	plausible maximum	typical average	plausible maximum	typical average
TYPICAL ONTARIO RESIDENT				
TYPICAL ONTARIO	2.55	0.913	2.44	0.867
DELORO ALONE				
WHOLE TOWN	4.21	0.501	1.21	0.146
ZONE 1	3.42	0.213	2.35	0.0605
ZONE 2	1.8	0.251	0.628	0.0695
ZONE 3	5.08	0.742	1.4	0.187
ZONE 4	2.48	0.454	0.787	0.118
DELORO INCLUDING BACKGROUND				
WHOLE TOWN	5.07	1.17	1.99	0.746
ZONE 1	4.19	0.814	3.13	0.661
ZONE 2	2.57	0.852	1.4	0.67
ZONE 3	5.86	1.34	2.17	0.787
ZONE 4	3.26	1.05	1.56	0.718

Table 5-15 Deterministic Incremental Lead Long-Term Exposure Ratio Values (preschool child) for Whole Town

	EXPOSURE RATIO VALUES	
	plausible maximum	typical average
Typical Ontario resident	2.14	0.753
Deloro alone (no home garden consumption)	1.21	0.146
Deloro alone (home garden consumption included)	4.29	0.570
Deloro including home garden consumption & background contribution	5.07	1.17

With the exception of the infant, the mean exposure estimates for Deloro residents not consuming home garden produce were less than the toxicological criterion (indicated by ER values less than 1.0), on a whole town basis as well as for each of the zones. The mean typical Ontario exposures for all receptors were also less than the toxicological criterion, although they were only marginally less for infants. Maximum exposure estimates for all residents in the typical Ontario scenario, and for infants, preschool children and children residing in Deloro, in the absence of home garden produce consumption, exceeded the toxicological criterion, which is based on induction of adverse neurological effects. Without the consumption of home garden produce, maximum and mean neurotoxicity risk estimates for typical Ontario residents exceeded those for Deloro residents.

For residents consuming home garden produce, mean exposure estimates exceeded the toxicological criterion for preschool children, while maximum exposures exceeded the toxicological criterion for all age classes of Deloro residents (*i.e.*, ERs were greater than 1.0). This was interpreted as indicating potential risk of impacts on neurobehavioural development in Deloro residents consuming home garden produce.

The major contributors to the risks to typical Ontario residents associated with lead were the general food basket and, to a lesser extent, drinking water. The contributors to overall risks for residents of Deloro (see Figures 5-14 and 5-15) indicated that the significance of contribution due to various exposure pathways was greatly dependent on receptor characteristics. Reviewing the predicted exposures in the absence of consumption of home garden produce, soil/dust ingestion contributed 45 to 60% of maximum risks for the infant and preschool child, and 20 to 25% of the mean risks, respectively. Again without home garden consumption, these pathways contributed 16 and about 2% of the maximum and mean overall risks for adults. Contributions to mean exposure *via* the general food basket ranged from about 71% for infants and preschool children to 90% for adults, while general food basket contributed about 25 and 50% to maximum exposures, for children and adults, respectively. Drinking water consumption provided a significant pathway of exposure (without home garden) as well, with consumption of Deloro municipal water contributing 10 to 20% of the maximum, and 1 to 2% of the mean risks for all receptors; similar but lower contributions were made by consumption of water from background sources. The greater

contribution to exposure to lead in drinking water from Deloro was due to the greater daily consumption within Deloro, as concentrations in Deloro municipal water were lower than background.

In summary, in the absence of home garden produce consumption, the main contributor to the maximum neurotoxicity risk estimates of young children was soil/dust ingestion, while the major contributor to the mean risk estimates of young children, as well as mean and maximum risk estimates of adults, was the general food basket. Drinking water, from Deloro and from background sources, also contributed significantly to these exposures in the absence of home garden produce consumption.

With the additional exposure pathway of consumption of home garden produce grown within Deloro, the ERs increased significantly. As will be discussed in Section 4.1.7, this exposure pathway contributed about 70% of the maximum overall exposures for all receptors, and about 30 to 40% of the mean overall exposures for all receptors. As discussed earlier, without home garden consumption, neurotoxicity risk estimates were lower for Deloro residents than for typical Ontario residents; however, the opposite was true when home garden consumption was included in the exposure estimate for Deloro residents. Figures 5-14 and 5-15 provide graphical examples of the above pathway contributions for both the mean and maximum preschool child home garden consumer receptors.

Given the exceedences of the toxicological criterion for residents of Deloro, and the exceedence of ERs for residents of Deloro in comparison to those of typical Ontario residents, it was concluded that the assessment of lead should progress to the probabilistic analysis.

4.1.5 Nickel

The risk characterization for nickel was based on endpoints of fetotoxicity following oral exposure and lesions of the lungs or nasal cavity following inhalation exposure. A review of the ER values predicted for nickel indicated that the infant was generally the most sensitive receptor for both mean typical Ontario and the overall risk estimates for Deloro residents. The ER values for the preschool child indicated that this receptor was also one of the more susceptible, and the plausible maximum ER for the preschool child was higher than that of the infant for background. The results of the risk characterization for the preschool child are provided in Table 5-16 and Figures 5-16 and 5-17.

Table 5-16 Deterministic Incremental Nickel Long-Term Exposure Ratio Values (preschool child) for Whole Town

	EXPOSURE RATIO VALUES	
	plausible maximum	typical average
Typical Ontario resident	28.6	17.9
Deloro alone (no home garden consumption)	1.21	0.271
Deloro alone (home garden consumption included)	3.02	0.577
Deloro including home garden consumption & background contribution	17.2	13.5

The mean and maximum exposures determined for nickel exposures, with and without consumption of home garden produce, were elevated above the toxicological criteria for exposures associated with typical Ontario, whole town and each of the zones. The ERs for overall exposure of Deloro residents were much less than those for exposures of a typical Ontario resident, and, indeed, the majority of risks predicted for Deloro residents were derived from background exposures (*i.e.*, the general food basket). Further examination of the background risks indicated that more than 95% of the background risk estimate was based on exposure *via* the general food basket, and therefore the risk estimate was a reflection of the oral toxicological criterion (based on fetotoxicity).

In terms of overall risk for residents of Deloro, the contribution of risks from consumption of general food basket decreases from greater than 90% for infants to about 75% for adults. This difference can be likely attributed to use of food consumption data which was not age-specific, that is, data more representative of food consumption patterns of adults, not infants. This would yield overestimations of intake of nickel *via* the general food basket for infants and preschool children, on a body weight basis.

The remainder of the risk for background was primarily due to inhalation; although actual exposures to nickel *via* inhalation were relatively small, the toxic potency of nickel for this route (based on lesions of the lung and nasal cavity) is high, resulting in a significant contribution to overall risk. Thus the elevation of risks in typical Ontario residents in comparison to Deloro was due to the higher range of concentrations reported for ambient air in Ontario.

The contribution of exposures to environmental media in Deloro to overall risk of Deloro residents was relatively minor, comprising about 10% or less of the mean and maximum total risk for all residents, with and without the consumption of home garden produce.

Given that mean and maximum typical Ontario risks exceeded the risks predicted for Deloro residents, and given that the majority of the risk indicated for Deloro residents was contributed by background sources, concentrations of nickel in Deloro environmental media

were not considered to pose an increased risk of adverse health effects, in comparison to typical Ontario.

4.1.6 Silver

The risk characterization for silver, based on induction of argyria, indicated that for estimates based on exposures of typical Ontario residents and total exposures of Deloro residents, the infant was the most sensitive receptor; based on exposures associated with Deloro alone, the preschool child was the most sensitive receptor. The results of the risk characterization for the preschool child are provided in Table 5-17 and Figures 5-18 and 5-19.

Table 5-17 Deterministic Incremental Silver Long-Term Exposure Ratio Values (preschool child) for Whole Town

	EXPOSURE RATIO VALUES	
	plausible maximum	**typical average**
Typical Ontario resident	1.02	0.624
Deloro alone (no home garden consumption)	0.0524	0.00843
Deloro alone (home garden consumption included)	0.291	0.044
Deloro including home garden consumption & background contribution	1.27	0.651

With and without the consumption of home garden produce, mean and maximum exposures for the whole town and each of the zones were less than the toxicological criterion (based on induction of argyria) for all receptors except the infant and the preschool child (as indicated by ERs less than 1.0). For the infant, both mean and maximum exposures slightly exceeded the toxicological criterion, while only the maximum exposure for the preschool child exceeded the toxicological criterion. Argyria risk estimates for Deloro residents were slightly greater than those calculated for exposures of a typical resident of Ontario.

Examination of exposure pathway contributions indicated that more than 99% of the background exposure and risk was through the general food basket for all receptors. In terms of overall risk, the contribution of the general food basket to risks for Deloro residents decreased from greater than 97% for infants to about 80% for adults. This variability was related to the data upon which the general food basket exposure to silver was based. Age-class specific estimates of dietary exposure to silver were not available, and therefore, an overall range of intakes, presumably based on food consumption patterns more representative of adults than children, was used. Adjusting these values to a per body weight basis would yield higher intakes of silver (as mg/kg body weight/day) for children than for adults. Therefore, this estimate of intake of silver *via* the general food basket for infants and preschool children may be conservative, and would likely have overestimated exposure and risk.

In the absence of home garden produce consumption, maximum exposures within Deloro contributed less than 10% to the overall maximum risks. With consumption of home garden produce, the contribution of exposures to environmental media within Deloro increased to 30% for maximum exposures, and about 10% or less for mean exposures. The majority of this increased contribution was due to exposures *via* home garden produce, which will be discussed in greater detail below.

For all receptors except the preschool child and infant, the maximum exposures were less than the toxicological criterion, with and without the consumption of home garden produce, while for the two youngest age classes, the exceedence was very marginal. As discussed in Part 4, Section 6.0, the toxicological criterion for silver is based on the induction of argyria, a blueish-grey discolouration of the skin, eyes and/or mucous membranes, a strictly cosmetic alteration of colouring which is not associated with any type of tissue damage or actual adverse health effect. Given that background contributions to risk, based mainly on a highly conservative estimate of intake *via* general food basket, especially for infants and children, comprised such a high proportion of the total risk, and that the exceedence of the toxicological criterion was marginal, it was concluded that concentrations of silver in environmental media in the village of Deloro would not result in a measurable increase in risk of adverse health effects.

4.1.7 Relevance of Exposures via Soil and Dust

The significance of contamination in indoor and outdoor soils and dusts within Deloro to the exposure and risk of its residents varied for each of the chemicals of concern. Direct exposure pathways for soil and dusts include accidental ingestion of soils or dust, inhalation of airborne particles, and dermal contact with soils. An indirect pathway of exposure to contaminants in soils, consumption of fruits and vegetables grown in home gardens, is discussed separately, in Section 4.1.8.

For cobalt, nickel and silver, the ingestion, inhalation and dermal exposure *via* indoor and outdoor soil/dust contributed relatively small proportions of overall risks of Deloro residents who also consumed home garden produce. Specifically, these pathways contributed approximately 4%, 3%, and 4%, to the overall risks associated with cobalt, nickel and silver, respectively.

For lead, direct exposure pathways for soils and dusts contributed up to approximately 11 to18% to overall risks of Deloro preschool children (see Figures 5-14 and 5-15). The primary contribution of soil-borne lead to overall risks is *via* consumption of home garden produce, which is discussed in the following section.

As was discussed earlier, the exposure to arsenic *via* direct pathways comprised a significant proportion of overall risk for Deloro residents. Children experienced relatively higher exposures *via* soil ingestion (contributing about 10% to overall risks) than did adults (contributing 2%). Contribution to overall risk by exposure *via* dermal contact was similar in both children and adults (5 to 25% and 10 to 20%, respectively, for mean and maximum

estimates). The significance of the dermal exposure pathway is somewhat unique to arsenic, based on the results of the current assessment; this is likely due to the higher dermal bioavailability of arsenic, which exceeds that of the other metals by 2- to 30-fold. This exposure may also be overestimated in the current assessment, because the range of dermal bioavailabilities of arsenic is representative of the differential bioavailabilities when administered in an aqueous (1.9%) or soil (0.8%) matrix. In order to be conservative, the higher of these two values was used; however, given that the exposure would be to soil-borne arsenic, it is likely that the exposure to arsenic *via* dermal contact with soil was overestimated by up to 2-fold. Using the lower value would not significantly alter the results of the assessment, but it would serve to slightly reduce the contribution of dermal contact to overall risk.

The importance of examining specific environmental media with respect to impacts on the overall risks for Deloro residents lies in the utilization of such information to guide risk management decisions. Therefore, as direct exposure pathways for soil/dust was identified in the deterministic analysis as contributing a potentially significant proportion of overall risk for arsenic, for both children and adults residing in Deloro, the importance of these pathways to risk estimation in the probabilistic analysis was also evaluated, as is discussed in Section 4.2. This allowed the incorporation of the more realistic modelling of the probabilistic analysis in development of risk management recommendations. Direct soil/dust exposures were not considered to be significant for lead, and thus did not need to be further examined.

4.1.8 Relevance of Consumption of Home Garden Produce

As is indicated in the preceding discussions, the contribution of the consumption of home garden produce grown in Deloro to estimates of overall risks varied considerably with the chemical under examination. While the contributions of home garden produce to overall risks associated with cobalt was less than 2%, risks from the consumption of home garden produce contributed approximately 60 to 70% of the maximum and 30 to 40% of the mean overall risks for lead, respectively. Intermediate contributions of home garden produce consumption are indicated for silver (25% and 10% contribution to maximum and mean risks), nickel (less than 15% and 4%, for maximum and mean risks, respectively) and arsenic (less than 2% contribution to mean and maximum overall risks).

The variation in the relative contribution of home garden produce is related to differences in 2 factors:

(i) the site-specific biotransfer factors (BTFs, discussed in Section 2.0); and,
(ii) the toxic potency of the element.

The contribution of produce consumption to arsenic risks also reflects the proportion of inorganic arsenic in vegetation. The estimate of intake of arsenic was modified from the BTF-based value for total arsenic to be predictive of the expected concentration of inorganic arsenic in fruits and vegetables, rather than that of total arsenic. This was based on literature values indicating that less than 10% of total arsenic is inorganic in several vegetable samples

(Pyles and Woolson, 1982; Weiler, 1987). As discussed in Part 4, Section 2, intake of inorganic arsenic is considered toxicologically significant while organic forms of arsenic are without adverse toxicologic effects.

The consumption of home garden produce included estimates of exposure through consumption of fruits, root vegetables, and other vegetables. Although there was a relatively high degree of variability in the site-specific BTFs, the site-specific data for green beans, lettuce and carrots were considered to be highly relevant to the prediction of concentrations in root and other vegetables. However, the relevance of these data to the estimation of concentrations in fruit is not known. Differences in basic physiology, including differences in root uptake and in the mass of edible portions relative to the mass of the entire plant, between fruits grown on trees or bushes, and vegetables such as beans, lettuce and carrots would suggest that application of the BTFs to fruits would likely overestimate concentrations in edible portions of fruit. Indeed, there were data in the literature for biotransfer of arsenic into apples (Aten *et al.*, 1980) which provided a BTF much lower than that for vegetables. Laul *et al.*, (1979) also observed that apples contain much lower concentrations of arsenic than do vegetables, when grown in soil not known to be contaminated by arsenic. Based on the assumption that the accumulation of metals in fruits would more closely resemble that for "other" vegetables (*i.e.*, beans and lettuce) than root vegetables, and because site-specific BTFs for other vegetables exceeded that of root vegetables, so did the BTFs for fruits. With correction to wet weight, fruits would be predicted to have greater concentrations than "other" vegetables as well, based on a lower percent moisture. The exceptions to this pattern were arsenic, for which a BTF for apples was used, and lead, for which the root vegetable BTF exceeded that for "other" vegetables and therefore fruits, and thus only for lead were predicted concentrations highest in root vegetables rather than fruit.

The subsequent relative contributions of the fruits versus vegetables (root and other) are dependent on the proportion of fruits and vegetables that were predicted to be obtained from a home garden, as well as the predicted concentrations. Based on these factors, it was determined that for cobalt, silver and nickel, consumption of home grown fruits contributed 40 to 50% of the risks associated with consumption of home garden produce. For risks associated with exposure to lead *via* home garden produce consumption, the contribution of fruits was much lower, about 20%. For arsenic, based on an actual fruit-based BTF (apples) the contribution of fruits was only about 3% of the risks associated with consumption of home garden produce.

In summary, then, consumption of root and other vegetables has been identified as potentially contributing significantly to overall risks for lead. Therefore, it was concluded that the evaluation of their significance should be reassessed in the probabilistic analysis, and the development of the risk management recommendations should take into consideration these contributions and the uncertainties in their estimation, as discussed above.

4.1.9 Relevance of Exposures via Trespassing on the Mine Site

Figures 5-20 to 5-25 present the predicted risks for residents exposed to contaminants on the mine property as a result of trespassing on the site in addition to consuming home garden produce. These risk are also presented as increments of other Deloro risks in Figures 5-6 and 5-13. In general, only for maximum risk estimates for arsenic (carcinogenic and non-carcinogenic endpoint) were there significant increases in the risk estimates following addition of the trespasser scenario. Contributions of trespasser exposures to mean predicted risks for arsenic were minimal, and the contributions of the trespasser scenario to mean and maximum risks for cobalt, lead, nickel, and silver were negligible.

There are concerns, however, about the validity of the use of the maximum concentrations of arsenic reported for the mine site. Reviewing these concentrations (see Appendix B) indicates extremely high concentrations which may be indicative of arsenic stockpiles (*e.g.*, maximums for the mine site indicated 22% arsenic in the sample by weight). It is unlikely that a resident hiking on the mine site would spend any prolonged period of time in contact with these areas of extreme concentrations, although the predicted maximum risks are based on the assumption that the receptor spends half an hour per day at the maximum concentration on the mine site. Additionally, the trespasser scenario considered direct contact soil related exposure pathways similar to those considered for the town. Soil-related exposures in town included the potential for playing and gardening in impacted soils in addition to walking in these areas, while it is expected that people will only spend time walking on the mine site. Therefore, it was concluded that the results for the trespasser scenario likely overestimated risks to Deloro residents by a significant a degree. However, it was concluded that the trespassing on the mine property may contribute significantly to the overall risks of Deloro residents, and therefore, mitigation of this exposure should be considered in development of the remediation plan for the site.

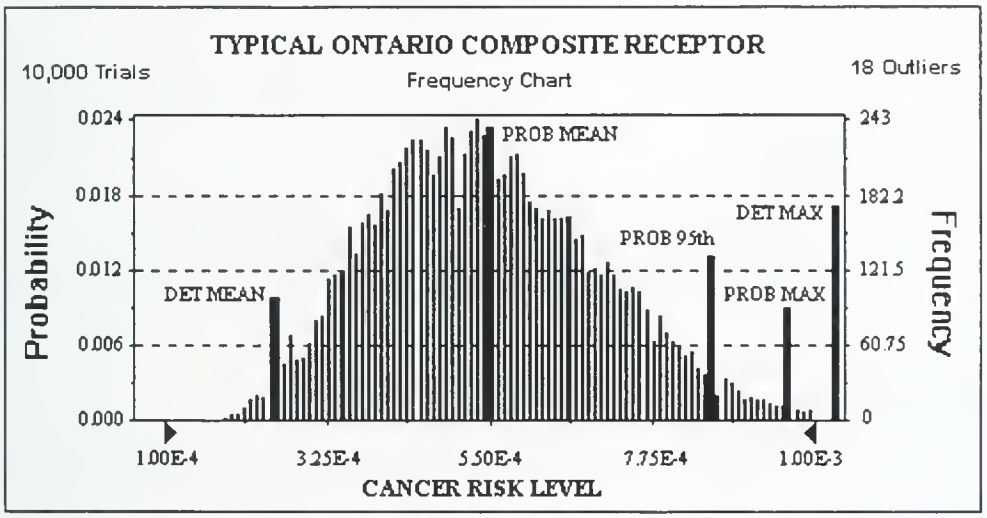
4.1.10 Conclusions of the Deterministic Analysis

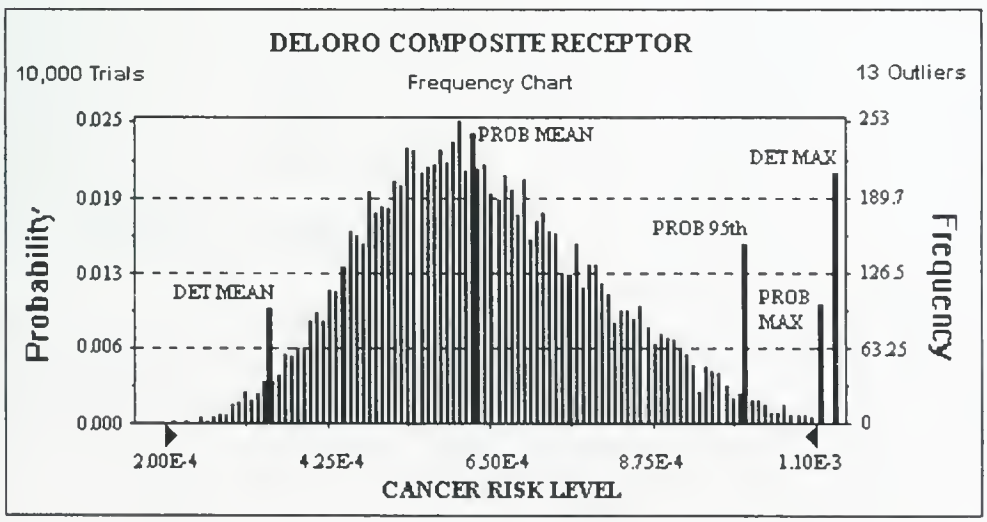
Based on the results of the deterministic analyses, as discussed above, it was concluded that arsenic (carcinogenic and non-carcinogenic) and lead should be carried forward for probabilistic analyses, based on predicted exceedences of the toxicological criterion and predicted risks for typical Ontario residents.

4.2 Probabilistic Analysis

The results of the probabilistic analysis of risks associated with exposures to arsenic and lead are presented in tabular and graphical form for the preschool child (non-carcinogens) and composite receptor (carcinogens). The following forecast charts are examples of the probability density function (PDF) characterizing the distribution of CRLs for carcinogenic arsenic risks for the composite receptor of Ontario and Deloro, following 10,000 iterations of the probabilistic model. The forecast chart demonstrates the actual shape of the distribution of risk estimates. While Figures 5-20 to 5-25 characterize the range between the 5th and 95th percentiles of the risk PDF, the forecast charts demonstrate the actual shape of the

distribution. PDFs for the other probabilistic modelling results (all receptors, arsenic and lead, home garden consumers and non-consumers) have a similar shape, as can be seen in comparing the distributions for Ontario and Deloro composite receptors (below). These results demonstrate that for both Ontario and Deloro residents, the 95th percentile of the risk estimate, which is typically used as the decision point in probabilistic risk assessments, is representative of only a very small segment of the population. In comparison, the risk estimates for the bulk of the population, which fall around the 50th percentile, tend to be much lower that the 95th percentile. As would be expected, based on the discussion of results earlier, the cancer risk estimates for Ontario residents are slightly lower than those for Deloro residents, which is reflected in the minor shift of the typical Ontario distribution curve to the left.





4.2.1 Arsenic (Carcinogenic)

The most sensitive receptor for risks associated with exposures to arsenic, based on carcinogenic endpoints, was the composite receptor, representing cumulative cancer risks over a lifetime. The CRLs for arsenic for the composite receptor are presented in Tables 5-18 and 5-19 and in Figures 5-26 and 5-27. The increments in total estimated cancer risks, comparing CRLs for typical Ontario residents, Deloro residents without consumption of home garden produce, and with home garden produce, are presented in Figure 5-28.

A comparison between the predicted risks for exposures to arsenic for typical Ontario residents and exposures of Deloro residents (without home garden produce consumption) indicated marginal increases in risk for residents of Deloro (about 0.2-fold greater than typical Ontario).

Table 5-18 Probabilistic Arsenic Estimated Lifetime Cancer Risk Levels (ALL CANCERS)

	ESTIMATED CANCER RISK LEVEL					
	Home Garden Consumption			No Home Garden Consumption		
	5th percentile	median	95th percentile	5th percentile	median	95th percentile
TYPICAL ONTARIO RESIDENT						
TYPICAL ONTARIO	3.19e-04	5.37e-04	8.17e-04	3.08e-04	5.39e-04	8.23e-04
DELORO ALONE						
WHOLE TOWN	6.57e-05	1.09e-04	1.79e-04	5.95e-05	9.84e-05	1.68e-04
ZONE 1	4.83e-06	8.15e-05	1.44e-04	4.76e-05	7.91e-05	1.43e-04
ZONE 2	5.42e-05	8.85e-05	1.55e-04	5.08e-05	8.42e-05	1.51e-04
ZONE 3	7.52e-05	1.34e-04	2.30e-04	6.82e-05	1.16e-04	1.99e-04
ZONE 4	7.84e-05	1.30e-04	2.06e-04	7.29e-05	1.16e-04	1.88e-04
DELORO INCLUDING BACKGROUND						
WHOLE TOWN	4.02e-04	6.27e-04	9.12e-04	3.84e-04	6.23e-04	9.08e-04
ZONE 1	3.74e-04	6.02e-04	8.86e-04	3.71e-04	5.95e-04	8.77e-04
ZONE 2	3.77e-04	6.11e-04	8.90e-04	3.76e-04	6.04e-04	8.83e-04
ZONE 3	4.28e-04	6.61e-04	9.40e-04	4.11e-04	6.36e-04	9.19e-04
ZONE 4	4.14e-04	6.41e-04	9.32e-04	4.13e-04	6.31e-04	9.19e-04

Table 5-19 Probabilistic Arsenic Estimated Lifetime Cancer Risk Levels (by cancer type) for Whole Town

	ESTIMATED CANCER RISK LEVEL		
	5th percentile	median	95th percentile
ALL CANCERS COMBINED			
Typical Ontario resident	3.19e-04	5.37e-04	8.17e-04
Deloro alone (no home garden consumption)	5.95e-05	9.84e-05	1.68e-04
Deloro alone (home garden consumption included)	6.57e-05	1.09e-04	1.79e-04
Deloro including home garden consumption & background contribution	4.02e-04	6.27e-04	9.12e-04
LUNG CANCERS			
Typical Ontario resident	2.94e-06	1.00e-05	1.89e-05
Deloro alone (no home garden consumption)	1.69e-07	3.76e-07	7.39e-07
Deloro alone (home garden consumption included)	1.69e-07	3.76e-07	7.39e-07
Deloro including home garden consumption & background contribution	1.04e-06	2.83e-06	5.28e-06
SKIN CANCERS			
Typical Ontario resident	3.04e-04	5.20e-04	8.02e-04
Deloro alone (no home garden consumption)	3.93e-05	9.81e-05	1.68e-04
Deloro alone (home garden consumption included)	6.48e-05	1.07e-04	1.83e-04
Deloro including home garden consumption & background contribution	3.92e-04	6.14e-04	9.10e-04

An analysis of the relative importance of the pathways of exposure in the probabilistic analysis are provided in Figures 5-29 through 5-31. Examination of the contributors to overall predicted risks from arsenic for Deloro residents (with consumption of home garden produce) in the probabilistic analysis indicated that the general food basket contributed more than 90% of the typical Ontario risks for the composite receptor, while drinking water and air contributed up to 6% and 2.4%, respectively. The general food basket was also the primary contributor of risk for Deloro residents (74 to 83% of overall risks for the composite receptor), while municipal drinking water, soil and indoor dust, and home garden contributed up to 14%, 6%, and 5%, respectively. While drinking water was a contributor to overall

risks, the concentrations of arsenic in Deloro municipal drinking water (3.62 µg/L) were well below the Ontario drinking water quality objective (25 µg/L).

Negligible or *de minimis* cancer risk level is generally considered to be 1 in ten thousand ($1x10^{-4}$) to 1 in one million ($1x10^{-6}$), and risk estimates for a population which are greater than this level would be considered to be elevated. However, when estimates of cancer risk for typical Ontario residents exceed this negligible level of risk, it would be expected that the estimated risks for any population within Ontario, such as the residents of Deloro, would also exceed the level considered negligible. This is evident in the current assessment, as the 95th percentile CLRs for typical Ontario residents were $8.17x10^{-4}$ for home garden consumers, while 95th percentile CLRs for Deloro residents ranged from $8.9x10^{-4}$ to $9.4x10^{-4}$ (whole town: $9.12x10^{-4}$), higher than typical Ontario by a factor of about 0.2-fold. The elevation of risk for typical Ontario residents would indicate an overestimation of risk due to a high degree of conservatism in the risk assessment; the elevation of risks to Deloro residents, in large part, would be due to the same conservatism.

Of considerable importance to the assessment of arsenic is the conservatism inherent in the dose-response relationship used in development of the cancer potency factor for arsenic by the U.S. EPA. The toxicological profile of arsenic, and specifically the estimation of its carcinogenic potency, has been discussed in detail in Part 4, Section 2. This conservatism would result in the overestimation of the potency of arsenic in inducing skin cancer, and consequently may lead to overestimation of predicted skin cancer risks, especially at lower rates of exposure more typical of most North American populations. To summarize briefly, the U.S. EPA cancer slope factor for oral exposures, which was utilized in the current assessment, is based on an epidemiological study of skin cancer in a Taiwanese population exposed to extremely high concentrations of arsenic in drinking water (more than 1 mg/L) (Tseng *et al.*, 1968; Tseng, 1977). There are some limitations of the Tseng studies, including uncertainties in the determination of actual exposure levels, inclusion of exposure from drinking water alone versus the possibility of exposure *via* diet, herbal remedies and other sources, concomitant exposures to other chemicals, and possible nutritional deficiencies of the diet. In general, the Taiwan data could be representative of a relatively sensitive population, whether due to nutrition, health status or genetics. The overestimation of risks for North American populations, demonstrated in epidemiological studies of cancer risk, would be related to differences in these parameters. The uncertainties in the Tseng *et al.* data and the impact of such uncertainties on the estimation of CRLs are discussed in further detail in Part 4, Section 2.4.5.

In the frame of reference of the current assessment, if the skin cancer potency of arsenic has been overestimated, then the risks of skin cancer predicted for the population of Deloro or Ontario would also have been overestimated in this assessment. Therefore, given that the same methodologies were used in estimating exposure and risk for typical Ontario residents and Deloro residents, the comparison of these two groups would be the most appropriate way of evaluating the risk estimates. To further put the risks predicted in this assessment into perspective, they can be compared to those predicted for other North American populations. Smith *et al.* (1993b) assessed the cancer risk of typical American populations, based on the

reported concentrations of arsenic in drinking water. Estimated CRLs for various populations, based solely on exposure *via* drinking water, were in the range of 1 in 1,000. As a quick comparison, a deterministic assessment of risks associated with drinking water at concentrations equal to the OMOE (1994c) criteria (25 µg/L) would yield a CRL of 1 in 1,250, based on the daily exposure of typical Ontario residents over a life time. The risks associated with exposure *via* general food basket would further increase the CRL to approach 1 in 1,000 as well. The OMOE (1996) has conducted an exposure assessment for Ontario residents and estimated CRLs of 1 in 1,500 for multimedia exposures, including drinking water, soil, general food basket and air, but not consumption of home garden produce. Given that based on actual cancer risk estimates, the typical Ontario resident is not considered to be at elevated risk of skin cancer from arsenic, the predicted risk for this population can provide a benchmark by which risks to Deloro residents may be evaluated, as has been done above. For example, the incidence of non-melanoma skin cancers (including but not limited to basal and squamous cell carcinoma) in Ontario can be estimated to be about 1/2000 (based on data cited in Statistics Canada, 1988; 1990); however, the vast majority of these cases would be attributable to damage caused by sunburn and blistering following excessive sun exposure. Other causal agents of non-melanoma skin cancer include occupational exposures, genetic predisposition, in addition to arsenic. While the specific proportion associated with arsenic exposure cannot be determined from these data, it is highly likely that actual arsenic-related skin cancer risks for typical Ontario residents would be less than 1 in 20,000.

With respect to risks associated specifically with direct exposure pathways to soil (ingestion, inhalation and dermal contact), it is useful to put Deloro soil concentrations into perspective by considering soil concentrations elsewhere. Whole town concentrations of arsenic in Deloro soils had a mean of 111 mg/kg, and a 95th percentile (considered to be the plausible maximum) of 308 mg/kg. In comparison, concentrations of arsenic in surface soils near smelting facilities such as Anaconda, Montana and ASARCO, Washington have been reported to range up to 2,000 mg/kg, and to have a range of mean concentrations of 50 to 420 mg/kg (within 0.3 km of the smelter) (see Part 3). Another Ontario community situated in the close proximity to a gold mine, Balmertown, had a range of concentrations of arsenic in surface soils similar to that of Deloro, although mean concentrations were slightly higher (means for garden soils were reported to be 58 to 163 mg/kg, perimeter and play area soils had means of 214 and 239 mg/kg, respectively) (Gradient Corporation, 1995). The results of the exposure assessment for this community indicated that food (including general food basket and home garden produce) contributed about 72% of overall risk, while drinking water and soil contributed approximately 20 and 8%, respectively. The authors further demonstrated through theoretical modelling that decreasing soil concentrations by half would result in a decrease in risks of skin cancer of only 2%.

Similarly, the probabilistic modelling effort was expanded to assess the impact of a decrease of soil/dust concentrations of arsenic resulting from the theoretical replacement of Deloro soils with typical Ontario soils. It was determined that this reduction of concentrations of arsenic in Deloro soils and dusts to levels considered to be typical for Ontario, would result in only a 2 to 4% reduction (for 95th and 5th percentiles, respectively) in the overall risks for the composite receptor. Therefore, it can be concluded that even if concentrations of arsenic

in soils and dusts were reduced to equal typical Ontario concentrations, there would likely be no measurable reduction of exposure, based on direct contact pathways. Home garden produce consumption represents an indirect exposure pathway to arsenic in soils; cessation of both this indirect pathway as well as the direct pathways would result in a reduction of up to 9%.

4.2.2 Arsenic (Non-Carcinogenic)

The risk characterization for arsenic based on non-carcinogenic endpoints was based on potential for induction of adverse skin effects (hyperpigmentation and keratosis). The most sensitive receptor for risks associated with exposures to arsenic, based on probabilistic analysis of risks of non-carcinogenic endpoints, was the infant. The results of this analysis are presented in Tables 5-20 and 21 and in Figures 5-32 and 5-33.

Table 5-20 Probabilistic Arsenic Long-Term Exposure Ratio Values (preschool child)

	EXPOSURE RATIO VALUES					
	Home Garden Consumption			No Home Garden Consumption		
	5th percentile	median	95th percentile	5th percentile	median	95th percentile
TYPICAL ONTARIO RESIDENT						
TYPICAL ONTARIO	0.745	2.35	5.15	0.735	2.31	5.07
DELORO ALONE						
WHOLE TOWN	0.203	0.508	1.29	0.180	0.480	1.24
ZONE 1	0.137	0.369	0.991	0.128	0.36	1.02
ZONE 2	0.152	0.401	1.04	0.148	0.382	1.04
ZONE 3	0.248	0.669	1.63	0.233	0.593	1.50
ZONE 4	0.268	0.631	1.47	0.230	0.580	1.41
DELORO INCLUDING BACKGROUND						
WHOLE TOWN	1.15	2.87	5.63	1.11	2.81	5.58
ZONE 1	1.02	2.75	5.52	1.01	2.75	5.48
ZONE 2	1.09	2.75	5.53	1.00	2.73	5.55
ZONE 3	1.26	2.99	5.85	1.23	2.97	5.88
ZONE 4	1.23	2.95	5.87	1.22	3.00	5.70

Table 5-21 Probabilistic Incremental Arsenic (non-cancer) Long-Term Exposure Ratio Values (preschool child) for Whole Town

	EXPOSURE RATIO VALUES		
	5th percentile	median	95th percentile
Typical Ontario resident	0.745	2.35	5.15
Deloro alone (no home garden consumption)	0.180	0.480	1.24
Deloro alone (home garden consumption included)	0.203	0.508	1.29
Deloro including home garden consumption & background contribution	1.15	2.87	5.63

The 5th percentile exposures for all typical Ontario receptors except the infant were less than the toxicological criterion, while the 95th percentile exposures for all typical Ontario receptors exceeded the toxicological criterion, as indicated by ERs of up to 5.15.

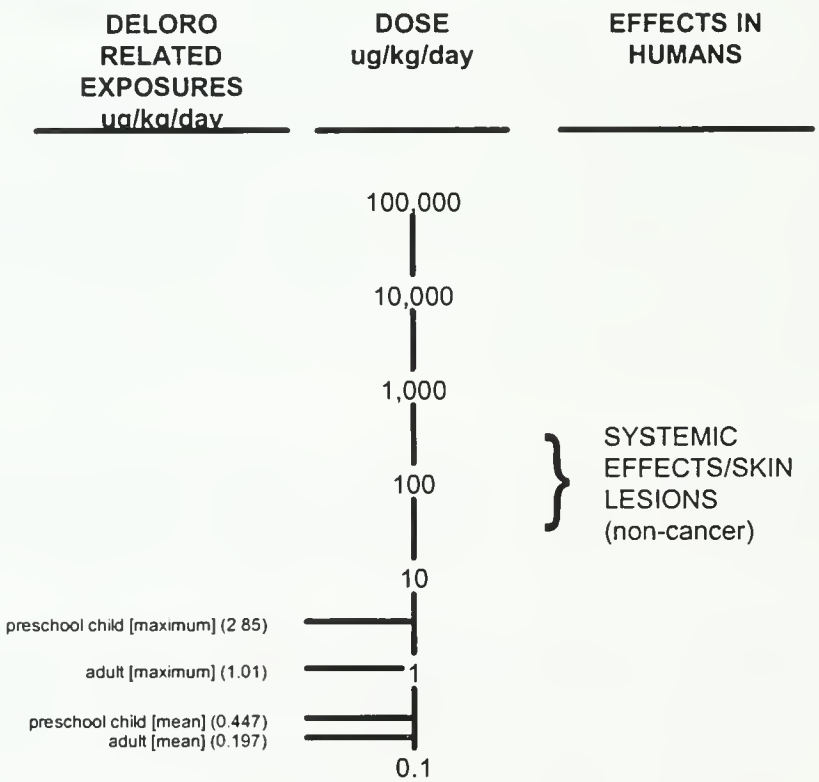
In the absence of consumption of home garden produce, the 95th percentile ER values for Deloro residents were elevated by about 0.2-fold over that of typical Ontario residents. 5th percentile exposures for infants and preschool children exceeded the toxicological criterion (the highest 5th percentile ER was 1.23), and 95th percentile exposures for all receptors exceeded the toxicological criterion, for the whole town and for each of the four Zones (highest 95th percentile ER was 5.88). Thus the risk of adverse skin effects (hyperpigmentation, keratosis) are only marginally elevated for Deloro residents, in comparison to typical Ontario residents.

As stated in Section 4.1.1, without consumption of home garden produce, contributors to Deloro-specific risks were municipal drinking water, dermal contact with soils/dusts and, for small children, dust and soil ingestion. With the consumption of home garden produce, ER values increased only minimally for Deloro residents (less than 0.1-fold).

The toxicological criterion for the non-carcinogenic endpoints of arsenic, derived by the U.S. EPA, is based on adverse skin effects (hyperpigmentation, keratosis). Other regulatory agencies have derived criteria to be protective of the non-carcinogenic endpoints of arsenic; Health Canada, for example, has promulgated a guideline protective of induction of symptoms of chronic arsenic poisoning of 2 µg/kg bw/d, as compared to the U.S. EPA value of 0.3 µg/kg bw/d. Although the more conservative value was employed in the risk assessment, use of the Health Canada guideline in the risk assessment would have resulted in the estimation of exposures for both Deloro and Ontario residents that were at or below the toxicological criterion (with a maximum 95th percentile of 0.84 for the whole town).

A graphical representation of the estimated exposures of Deloro residents in comparison to the range of doses observed to cause adverse non-cancer effects in humans is provided below

(adapted from ATSDR, 1992). The occurrence of systemic effects and/or skin lesions in human populations exposed to arsenic has been associated with exposure levels much higher than those predicted for Deloro residents. Another consideration regarding the characterization of risks of adverse skin effects caused by arsenic involves the etiology of the skin condition itself. For example, although the highest risks were predicted for preschool children, there is little or no chance that skin effects would be seen in these receptors. Skin lesions and symptoms of the skin conditions associated with arsenic have not been observed in children less than 11 years of age, even when exposed to extremely high drinking water concentrations (U.S. EPA, 1998). The induction of the skin condition requires sustained, high-level exposures to arsenic, and the actual risks of skin effects are more likely to be reflected by the predicted risks for teenagers and adults. In addition, the toxicological criterion for the induction of adverse skin effects by arsenic are based on the Taiwan studies by Tseng *et al.*, and are thus limited by the same uncertainties as were discussed previously, including likely underestimation of dose (and thus overestimation of potency), nutritional deficiencies, and possible concomitant exposures to other chemicals.



4.2.3 Lead

The risk characterization for lead, based on potential impacts on neurobehavioural development, indicated that the preschool child was the most sensitive receptor for lead with consumption of home garden produce, while the infant was slightly more sensitive in the absence of home garden produce consumption. The results of the probabilistic risk

characterization for lead are provided in Table 5-22 and 5-23 and Figures 5-34 and 5-35. The increments in total risks, comparing ERs for typical Ontario residents, Deloro residents without consumption of home garden produce, and with home garden produce, are presented in Figure 5-35.

Table 5-22 Probabilistic Lead Long-Term Exposure Ratio Values (preschool child)

	EXPOSURE RATIO VALUES					
	Home Garden Consumption			No Home Garden Consumption		
	5th percentile	median	95th percentile	5th percentile	median	95th percentile
TYPICAL ONTARIO RESIDENT						
TYPICAL ONTARIO	0.761	0.993	1.59	0.658	0.829	1.39
DELORO ALONE						
WHOLE TOWN	0.181	0.626	1.95	0.0428	0.16	0.545
ZONE 1	0.0802	0.278	0.826	0.0237	0.0949	0.304
ZONE 2	0.140	0.643	2.21	0.0323	0.152	0.572
ZONE 3	0.365	1.10	3.45	0.0579	0.227	0.845
ZONE 4	0.196	0.498	1.27	0.0371	0.135	0.419
DELORO INCLUDING BACKGROUND						
WHOLE TOWN	0.798	1.25	2.59	0.646	0.789	1.23
ZONE 1	0.692	0.909	1.49	0.625	0.724	0.989
ZONE 2	0.752	1.27	2.87	0.634	0.781	1.24
ZONE 3	0.974	1.73	4.10	0.657	0.857	1.52
ZONE 4	0.806	1.13	1.93	0.637	0.761	1.10

Table 5-23 Probabilistic Incremental Lead Long-Term Exposure Ratio Values (preschool child) for Whole Town

	EXPOSURE RATIO VALUES		
	5th percentile	median	95th percentile
Typical Ontario resident	0.658	0.829	1.39
Deloro alone (no home garden consumption)	0.0428	0.16	0.545
Deloro alone (home garden consumption included)	0.181	0.626	1.95
Deloro including home garden consumption & background contribution	0.798	1.25	2.59

Estimated exposures for typical Ontario infants, preschool children and children ranged from below the toxicological criterion for the 5th percentile results to slightly in exceedence of the limit for the 95th percentile, as indicated by the ER values in the tables above. 5th and 95th percentile exposures for typical Ontario adolescents and adults were both less than the toxicological criterion.

For Deloro residents, in the absence of exposure to lead through the consumption of home garden produce, the 5th and 95th percentile ERs were slightly less than those reported for typical Ontario exposures for all receptors except the infant. While 5th percentile ER values for the infant resident of Deloro village were less than typical Ontario residents, the 95th percentile values for the infant for the whole town and, Zones 2 and 3 were marginally in exceedence of typical Ontario 95th percentiles. These increases were slight, however, representing an increment of less than 1.5-fold. Further, these increments were observed only for the infant, and, as stated in Section 4.1.4, would be mainly due to ingestion of soils and dusts. Given that the estimation of soil/dust ingestion by the infant was based on values (in g per day) reported for preschool children, the contribution of this exposure pathway is likely overestimated for the infant. Soil/dust ingestion more accurately portrays exposure of the preschool child, for which there were no elevations in overall risk in Deloro. Therefore, in the absence of consumption of home garden produce, exposures to lead in environmental media within Deloro were not considered to increase overall risks of residents, and would not be associated with a measurable increase in risks of neurological effects.

The major contributors to the risks to typical Ontario residents associated with lead were the general food basket and, to a lesser extent, drinking water. The contributors to overall risks for residents of Deloro indicated that the significance of contribution due to various exposure pathways was greatly dependent on receptor characteristics. Reviewing the predicted exposures in the absence of consumption of home garden produce, soil/dust ingestion contributed 45 to 60% of maximum risks for the infant and preschool child, and 20 to 25% of the mean risks, respectively. Again without home garden consumption, these pathways contributed 16 and about 2% of the maximum and mean overall risks for adults.

Contributions to mean exposure *via* the general food basket ranged from about 71% for infants and preschool children to 90% for adults, while general food basket contributed about 25 and 50% to maximum exposures, for children and adults, respectively. Drinking water consumption provided a significant pathway of exposure (without home garden) as well, with consumption of Deloro municipal water contributing 10 to 20% of the maximum, and 1 to 2% of the mean risks for all receptors; similar but lower contributions were made by consumption of water from Ontario sources. The greater contribution to exposure to lead in drinking water from Deloro was due to the greater daily consumption within Deloro, as concentrations in Deloro municipal water were one fourth to one seventh of the values report for Ontario drinking water.

With the consumption of home garden produce, the ER values for Deloro residents were slightly less than 2.5-fold greater than those of non-consumers. While 5th percentile exposures remained less than the toxicological criterion for all receptors, 95th percentile exposures exceeded the toxicological criterion for all receptors in the whole town and Zones 2 and 3. The consumption of home garden produce contributed about 40% of the overall mean risks, respectively, to Deloro residents (about 70% of maximum risks). Further examination of contributors to exposure *via* home garden produce indicated that about 80% was derived from consumption of root and "other" vegetables. Other pathways correspondingly decreased in proportional contribution, with general food basket about 50%, soil/dust pathways about 10%, and drinking water about 2% of the overall risks.

The maximum probabilistic ER value for lead of Deloro residents consuming home garden produce was 4.10 (the value predicted for residents of Zone 3), while the 95th percentile ER value for the whole town was 2.59. Although this is indicative of exposures exceeding the criterion based on neurological effects, an exceedence of this magnitude was not considered to be of concern, given the conservatism inherent in this risk assessment. The toxicological criterion is based on the lowest effective blood lead level reported in epidemiological studies of the effects of lead in human infants, who are considered to be the most sensitive receptors, based on both their susceptibility to neurodevelopmental effects as well as their higher gastrointestinal absorption of lead. In addition, the estimation of risks specifically to consumers of home garden produce was considered to be conservative for several reasons. These include the use of the entire range of concentrations throughout Deloro in the estimation of exposure included concentrations, not just those in back yards and gardens. Because home garden produce is more likely grown in these areas, which had lower concentrations, actual exposures and risks are expected to be lower. Based on this overestimation, and on the minimal increase in risks, the exposures to lead from consumption of home garden produce is not expected to measurably increase risks to Deloro residents.

To put the surface soil concentrations of lead in Deloro into perspective, they can be compared to concentrations found elsewhere in Ontario. MOEE (1994b) reported that the concentrations of lead in urban soils ranged from 5 to 845 mg/kg, and averaged 123 mg/kg, while the range in small towns was 2 to 133 mg/kg and the average 73 mg/kg. In comparison, the lead concentration in Deloro surface soils averaged 121 mg/kg, and ranged up to 655 mg/kg, in general agreement with the reported concentrations in urban soils. As

was discussed in the exposure assessment, because the range of concentrations in gardens or backyards (where gardens might be located in future) was not known, it was assumed that a garden could be located anywhere in Deloro, and that the whole town maximum would be representative of maximum garden soil concentrations. However, reviewing the soil concentration data in greater detail indicates that the maximum concentration in established gardens or in backyards is 250 mg/kg. In comparison, the maximum concentration in Deloro was 383 mg/kg, while the plausible maximum concentration was 344 mg/kg.

Weitzman *et al.* (1993) studied the changes in PbB of urban children following measures to abate direct soil exposures. Slight reductions in PbB were observed (a decrease of 0.8 to 1.6 µg/dL from an average of 13 µg/dL) following clean-up of interior dust and outdoor soils (concentrations in soil were reduced from about 2,000 mg/kg to about 105 mg/kg). It was concluded that based on the minimal reduction in PbB, soil lead abatement would not likely be beneficial in reducing PbB in urban children with low-level lead exposure.

The importance of exposure to lead *via* direct soil pathways to overall risks of typical Ontario residents was also examined by the OMOE (MOEE, 1994b). The toxicological criterion for lead was developed by the OMOE based on the acceptable blood lead concentration (PbB) of 10 µg/dL, specifically protective of neurotoxicity in infants. Extrapolation to acceptable daily intakes was based on a slope factor for describing the relationship of PbB and exposures of infants, that is, concentrations of lead in milk/formula. Therefore, the toxicological criterion is reflective of the bioavailability of lead ingested in milk or formula, as opposed to the bioavailability associated with soil-borne lead. Using the acceptable PbB of 10 µg/dL, the risk characterization may be re-visited using a model describing the relationship between PbB and exposure *via* all relevant exposure pathways. MOEE (1994b) reviewed two such models, the Integrated Uptake/Biokinetic Model (IU/BK), which calculates PbB based on environmental media concentrations, and the Society for Environmental Geochemistry and Health Model (SEGH), which relates soil concentrations to PbB. The MOEE determined that the SEGH model would predict that concentrations of up to 880 mg/kg would not result in PbB levels above the acceptable level for 95% of the population. The MOEE used the IU/BK model to test the sensitivity of PbB to changes in soil concentrations, given typical Ontario exposures *via* other pathways (food, drinking water, air). It was observed that, at bioavailabilities of 17% (similar to the bioavailabilities of 14 and 19% used for dust and soil in the current assessment), soil concentrations would have to exceed 600 mg/kg in order to cause PbB to exceed the acceptable limit of 10 µg/dL in children. This value does not appear to consider the consumption of home garden produce, however, the results of both models further support the conclusion of the current assessment that in the absence of home garden produce consumption, there was no measurable impact of Deloro-specific exposures on overall exposure and risk of Deloro residents.

5.0 URINARY ARSENIC EVALUATION

Generally, depending on the method of analysis, total urinary arsenic measurements include all forms of arsenic (*i.e.*, As(III), As(V), monomethylarsonic (MMA), dimethylarsinic acid (DMA) and organoarsenic such as arsenobetaine and other trimethylated forms). The toxicity of arsenic is primarily associated with inorganic species, and while organoarsenicals and trimethylated arsenic compounds can be present at high concentrations in seafood, they are not considered to be relevant for toxicological risk assessments (Gebel *et al.*, 1998, Walker and Griffin, 1998). Various studies have observed significant increases in total urinary arsenic levels after the consumption of seafood, however in general, have reported no significant increase in As(III), As(V), MMA and DMA levels (*e.g.*, Buratti *et al.*,1984), as discussed in greater detail in Part 4.2. However, other studies have indicated increases in speciated urinary arsenic following consumption of seafood including codfish, kelp, and bivalves (Le *et al.*, 1994; Goessler *et al.*, 1997; Gebel *et al.*, 1998; Le and Ma, 1998).

Therefore, while it may overestimate exposure for seafood consumers, speciated urinary arsenic is the recommended biomarker for recent (*i.e.*, 1 to 3 days) environmental and/or occupational exposure to inorganic arsenic (Walker and Griffin, 1998). When assessing exposures to inorganic forms of arsenic, it is crucial that the analytical methods used can distinguish between the non-toxic organoarsenicals and the toxicologically relevant forms and their metabolites (As[III], As[V], MMA and DMA), either as a group or separately (Farmer and Johnson, 1990). There are no objective criteria for evaluation of health status based on urinary arsenic levels, however, urinary arsenic levels of a chronically exposed population can be very helpful in a weight-of-evidence evaluation of health status. For further details regarding the metabolism and excretion of arsenic, as well as the use of urinary arsenic as a bioindicator, refer to Part 4, Section 1.4.

The objectives of this phase of the risk assessment were two-fold. The first was to validate the urinary arsenic exposure model. The second goal was to provide a basis for the evaluation of the exposure of Deloro residents in comparison to levels of arsenic in urine typical of Ontario residents (represented by Havelock). Urine samples taken from the town of Havelock (located about 20 km east of Deloro) were to represent typical Ontario urinary arsenic concentrations and were not considered to be impacted by the former mine site.

5.1 Measurement of Urinary Arsenic

Goss-Gilroy Inc. undertook the biomonitoring phase of the current assessment of Deloro residents. Biomonitoring results were reported for both total urinary and speciated urinary arsenic. Because of concerns regarding possible exposures to other forms of arsenic, the total urinary arsenic data were examined with regard to relation to seafood intake. Investigations of the total urinary arsenic data from Deloro participants have indicated a statistically significant increase in total urinary arsenic levels associated with those individuals who indicated recent fish and or seafood consumption (using the non-parametric Mann-Whitney U-Test). Therefore, for the purpose of the current assessment, the focus of this analysis has been confined to speciated urinary arsenic measurements as a bioindicator of recent inorganic

arsenic exposure. Table 5-24 summarises the speciated urinary arsenic concentrations of residents (*i.e.*, children under 12 years and adults) of Deloro and Havelock.

Table 5-24 Summary Table of Speciated Urinary Arsenic of Children (≤12 years) and Adults of Deloro Village and Havelock

	Children		Adults	
Statistic	**Deloro Village**	**Havelock**	**Deloro Village**	**Havelock**
INCLUDING NON-DETECT DATA (assumed concentrations below detection equalled ½ the detection limit)				
Mean	5.34	7.01	4.02	3.85
N	26	8	88	39
Standard Deviation	5.59	4.44	3.28	3.1
EXCLUDING NON-DETECT DATA				
Mean	15.21	11.04	12	14.4
N	5	2	11	3
Standard Deviation	6.77	1.71	4.82	2.88

Goss-Gilroy Inc. has completed a detailed analysis of these data; the following is a brief summary of data pertinent to this discussion. Total and speciated urinary arsenic levels of the residents of Deloro Village and residents in Havelock were compared. A total of 121 samples were obtained from Deloro residents, while 54 samples were obtained from Havelock residents. Following analysis of the urine samples, it was observed that a vast majority of samples were less than the detection limit (6 µg of arsenic / L of urine). Thus, the statistical analyses of these data were conducted in two ways: (i) including non-detect data (assuming that concentrations below detection were equal to 3 µg/L, or one-half of the detection limit), and (ii) excluding non-detect data.

5.2 Modelling Urinary Arsenic Concentrations

In order to support a meaningful comparison between biological monitoring data (*i.e.*, urinary arsenic concentration) and predicted exposure estimates (µg/kg body weight/day), data should be expressed in a common unit. Therefore an extrapolation from daily absorbed exposure predictions (µg/kg body weight/day) to estimated urinary arsenic levels (µg/L) is generally required. To allow for a comparison between estimated daily absorption (mg/day) and urinary arsenic levels (µg/L), Walker and Griffin (1998) used the following relationship:

$$EXC = (ABS \times CF_{abs}) / (RATE \times CF_{exc})$$

Where:

EXC	=	Urinary arsenic excreted (µg/L)
ABS	=	Estimated absorbed arsenic per day for each person (mg/day)
CF_{abs}	=	(1000 µg/mg); conversion factor
RATE	=	Estimated Urinary output per day (mL/day)
CF_{exc}	=	(0.001 L/mL); conversion factor

This relationship inherently assumes that 100 percent of the estimated daily absorbed intake is completely excreted *via* the urine on a daily basis. Studies have shown that at equilibrium, 40 to 60 percent of the absorbed ingested inorganic arsenic dose is excreted on a daily basis (Buchet *et al.*, 1981a,b; Farmer and Johnson, 1990). Therefore the following methodology was used to predicted urinary arsenic levels in the town of Deloro:

$$EXC = (ABS \times DIS \times BW) / (RATE)$$

Where:

EXC	=	Estimated Urinary Arsenic Concentration (µg/L)
ABS	=	Estimated absorbed arsenic (µg/kg bw/day)
DIS	=	Fraction of Urinary Arsenic Excreted Daily (unitless)
BW	=	Age Specific Body Weight (kg)
RATE	=	Reported Urinary Output per day (L/day)

The estimated absorbed arsenic was determined in the course of the human health risk assessment, based on exposures to environmental media as discussed in Section 2.0. As indicated previously, it has been estimated that 40 to 60 percent of the absorbed ingested inorganic arsenic dose is excreted on a daily basis at equilibrium. Therefore, for the current assessment, an estimated daily excretion factor for absorbed inorganic arsenic was considered to be 50 percent for a typical mean and 60 percent for a plausible maximum estimate. Urinary output rates for children less than 36 months of age and between 36 and 60 months of age were reported by Walker and Griffin (1998) to be 240 mL/day and 355 mL/day, respectively. This data was used to approximate the urinary output of infants and preschool children, respectively. A urinary output of 700 mL/day, reported by (ICRP, 1975) was used to represent children (5 to 12 years), while an excretion rate of 1.4 L/day were used for adolescent and adult receptors.

The resulting point estimate and probabilistic speciated urinary arsenic estimates for Deloro adults and preschool children, in addition to typical Ontario residents have been summarised in Table 5-25.

Table 5-25 Summary of Predicted Speciated Urinary Arsenic Concentration

Receptor	Plausible Max (Deterministic) µg/L	Typical Mean (Deterministic) µg/L	Probabilistic Median (*i.e.* 50th Percentile) µg/L	Probabilistic Upper Estimate (*i.e.* 95th Percentile) µg/L
Deloro Adult[1]	35.9	5.86	7.83	14.9
Deloro Adult	31.4	5.33	7.03	13.9
Typical Ontario Adult	18.4	3.86	5.63	12.3
Deloro Preschool Child[1]	94.6	12.9	20.6	44.5
Deloro Preschool Child	80.6	11.3	18.7	41.9
Typical Ontario Preschool Child	54.2	6.83	14.6	37.7

[1] Indicates the exposure *via* consumption of home grown produce within the town of Deloro.

Two estimates for typical Deloro adults and preschool children have been reported; the first estimate predicts urinary arsenic concentrations for those Deloro receptors who consume some proportion of their daily fruit and vegetable intake from their backyard gardens. The second estimate represents those receptors who do not consume home grown produce. Typical Ontario residents (as detailed in Section 1.0) were assumed to eat some portion of their daily fruit and vegetable intake from backyard gardens.

As illustrated in the previous equation, urinary arsenic concentrations are directly proportional to the daily absorbed dose (*i.e.*, µg/day) and inversely proportional to the daily urinary output rate (L/day). Due to a lack of age-specific urinary output data, single point estimate output rates (as outlined above) were used to help characterize all scenarios (*i.e.*, the typical mean, plausible maximum and probabilistic urinary arsenic measurements). Hence, the five-to-six fold difference observed between the plausible maximum and typical mean urinary arsenic concentrations were a result of the corresponding exposure estimates.

Typical mean urinary arsenic concentrations predicted for preschool children (age 6 months to 4 years) were approximately 2-fold higher than those estimated for adults. Because the ratio of exposure estimates for preschool and adults was equivalent it can be concluded that the differences in urinary arsenic concentrations between children and adults were due to differences in predicted exposures. Although daily urinary excretion rates affect the predicted urinary arsenic concentrations, and while there may be uncertainty in the accuracy of the values used in representing Deloro residents, it can be concluded that any variances were represented consistently across the age classes.

5.3 Results And Discussion

5.3.1 Urinary Arsenic Measurements

In these discussions, the levels of arsenic in urine is referred to on a volume basis, as opposed to a creatinine basis, as provided by Goss-Gilroy Inc. This was considered acceptable as sampling protocol ensured that first void samples (*i.e.,* first urination in the morning) were not included in the dataset. It was concluded that the level of dilution of urine would thus not range widely, and this assumption was borne out by statistical analysis which indicated that there were no differences in urinary arsenic concentrations in Deloro and Havelock residents when expressed on both a volume and on a creatinine basis.

A non-parametric Kruskal-Wallis test revealed there were no significant differences of total and speciated urinary arsenic levels between residents in Deloro Village and residents in Havelock whether data for samples with concentrations less than the detection limit was included or not. Similarly, comparisons were completed for each of the four zones within the Deloro Village, none of which revealed any significant differences of total and speciated urinary arsenic levels between residents residing in any zone of Deloro Village and residents in Havelock whether data for samples with concentrations less than the detection limit were included or not.

Knowing that the majority of samples fall below the detection limit of 6 μg/L reaffirms that during this "snap shot" in time (*i.e.*, 1 to 3 days prior to sampling), the population of Deloro were not experiencing exposure to arsenic outside that of a typical "background" population, as discussed above. However, not knowing the actual concentration of this fraction of the population results in a high level of uncertainty associated with the statistical characterization of the measured urinary arsenic data set. For the first comparison, half the detection limit was assumed, whereas in the second comparison, samples with concentrations less than the detection limit were excluded. By not including these samples, the reported urinary arsenic concentrations for Deloro Village (*i.e.,* those used for the second comparison) would most likely be an overestimate of the actual urine levels present in the town of Deloro. However, assuming half the detection limit (*i.e.*, 3 μg/L) for these samples and thus including them in the data set is most likely a more reasonable and realistic approximation of the actual urinary arsenic concentrations present in the village of Deloro. If a lower detection limit were to be used in determination of speciated urinary arsenic, presumably a much greater number of samples would have speciated urinary arsenic concentrations above detection, thus decreasing the current level of uncertainty associated with this data set.

In addition to this comparison to Havelock, the measured urinary arsenic concentrations were compared to concentrations reported in the published literature (Figure 5-37). The range of mean speciated urinary arsenic concentrations for residents of communities without known point sources of arsenic was 4.4 to 29 μg/L, with an average of 8 μg/L (see Part 3 for further details). In comparison, the range of speciated urinary arsenic concentrations in persons in the vicinity of mines or smelters was 8 to 280 μg/L (average approximately 52 μg/L), while

persons exposed to other point sources (occupational, drinking water) was 44 to 934 µg/L (average 233 µg/L).

The mean urinary arsenic concentrations of residents from both Deloro and Havelock fall in the range of typical background areas, and were much less than the means reported for persons exposed to point sources of arsenic.

5.3.2 Validation of Urinary Arsenic Model

In order to validate the exposure and urinary arsenic modelling, the measured values were also compared to the predicted concentrations. Figures 5-38 and 5-39 illustrate the comparison between predicted speciated urinary arsenic concentrations (for adults and children residing in the village of Deloro) versus measured speciated urinary data taken from approximately 140 Deloro residents.

In general, the measured and predicted urinary arsenic concentrations showed reasonable agreement. Figure 5-38 shows the results for adults, and indicates that the predicted values for Deloro residents with and without home garden consumption fall between the two data sets (with and without non-detect samples). The predicted values for children were somewhat higher than that for adults, and tended to exceed the measured urinary arsenic concentration for children from Deloro (Figure 5-39). This may be partially due to several factors: the relatively small samples size of children in Deloro, the relatively high detection limits associated with the measured data, as well as the inherent conservative of the predictive modelling. This general agreement between predicted and measured urinary arsenic concentrations can be interpreted as a validation of both the exposure assessment modelling and the urinary arsenic modelling. As discussed in Section 4.0, the major contributor to overall inorganic arsenic exposures for Deloro residents was background sources (general food basket). Municipal drinking water was another significant source. Therefore it would be expected that since exposures of the typical Ontario resident from background sources is similar to that of Deloro residents, there would be a good agreement between the measured urinary arsenic concentrations as well. The slight overestimate of predicted speciated urinary arsenic concentrations for children, was seen in the children of Deloro as well as typical Ontario children (see Table 5-25). Again, this consistency would be expected, as general food basket was a source common to both populations. The apparent over estimation of urinary arsenic concentrations and thus of overall modelled exposure may be due to an overestimate of exposure *via* the general food basket. As will be discussed in greater detail in Section 6.0, the upper range of intake of arsenic through general food basket was that derived by Environment Canada (1993) assuming 37% of arsenic in food is inorganic, however, several other studies of daily dietary intake of inorganic arsenic indicate much lower estimates, especially for children (Dabeka *et al.*, 1993; Yost *et al.*, 1998; MOEE, 1994a).

In conclusion, the results of the urinary arsenic model based on exposures associated with current conditions within Deloro and typical Ontario, showed good agreement with the measured concentrations for people living in Deloro and Havelock, which reflect recent

exposures to inorganic arsenic. There was a slight overestimation of urinary arsenic concentrations by the urinary arsenic model, which suggests that the exposure assessment modelling was based on conservative values and assumptions. This implied conservatism may be due to the overestimation of exposures associated with typical behaviours, but may also reflect alteration of behaviour in citizens who have responded to concerns over contamination in their village by minimizing exposure to contaminated media. Since the urinary arsenic model relied on the same exposure model as was used in estimating risks from exposure to arsenic, it is reasonable to conclude that the characterization of potential health risks from exposure to arsenic was also conservative. The good agreement between the urinary arsenic monitoring and the results of the risk assessment supports the conclusion that the residents of Deloro are not being subjected to measurably increased risk of cancer in comparison to the rest of Ontario.

6.0 UNCERTAINTY AND SENSITIVITY ANALYSIS

Environmental risk assessments typically simulate the highly complex chemical, biological, and physiological processes through which chemicals may affect people. Given the complexity of these processes, quantification of the potential risks associated with these impacts are associated with varying degrees of inherent uncertainty, dependent on the selection of parameters and equations to describe the various phases of exposure, hazard and risk assessment.

The term uncertainty usually incorporates both variability, a reflection of the heterogeneity or diversity observed in a well-characterized population, and uncertainty, which reflects limitations in the knowledge about a site, scenario or receptor. This lack of knowledge may be due to data gaps, randomness or unpredictability, measurement and systematic error, limitations of numerical modelling, toxicological uncertainty and/or decision rule uncertainty. An essential part of the interpretation of the results of a risk assessment is the consideration and, if possible, the quantitation of these sources of uncertainty.

The culmination of the uncertainty and sensitivity analysis is the identification of both the factors driving the risk assessment (*i.e.*, to which the risk estimate is most sensitive), and the level of uncertainty inherent in the values used in that risk estimate. If the sensitivity analysis indicates that a certain parameter has a significant impact on the calculation of risk, and the uncertainty analysis indicates that the value of this parameter is unsure, then the assumptions used to derive that value may need to be re-assessed. In such cases, uncertainty in the parameter may be mitigated by obtaining more data, or the uncertainty in the risk characterization may be addressed through consistent conservatism.

Pathway analysis, as discussed in Sections 5.4 and characterized in Figures 5-14, 5-15 and 5-29 through 5-31, helps to demonstrate which exposure pathways are the most significant contributors to the final risk estimate. On the other hand, sensitivity analysis helps to characterize which parameters are the most significant contributors to uncertainty in the probabilistic portion of the risk assessment. Sensitivity analysis helps to determine if the risk assessment is adequately conservative. These factors help to define the need for and course of mitigation at a site such as Deloro.

Sensitivity analyses consist of a qualitative or quantitative summary of the uncertainties associated with each input variable and a prediction of how these uncertainties are expected to affect the model outcome. To attempt to quantify the potential uncertainty within the current assessment, a sensitivity analysis was conducted for several selected "representative" receptors and scenarios at Deloro. The results of this sensitivity analysis (shown below) displays relative effects (contribution to variance) of key parameters on the outcome of the probabilistic risk assessment. Parameters with an effect correlation of less than 5% are not believed to exert a significant influence on the model outcome. Sensitivity results are provided for Background and Deloro (whole town) combined for the following situations:

(i) contribution of each receptor group to the variance in the composite receptor CRLs for arsenic (carcinogenic) (Figure 5-40);

(ii) contribution of each exposure pathway to the variance in the arsenic CRLs for the composite receptor group (home garden consumer) (Figure 5-41);

(iii) contribution of each probabilistic assumption to the variance in the arsenic CRLs for the adult receptor group (home garden consumer) (Figure 5-42); and,

(iv) contribution of each probabilistic assumption to the variance in the lead ER value for the preschool child receptor (Figure 5-43).

As noted below, the adult receptor contributed the most variance to the composite receptor risk estimate for arsenic (carcinogenic). This would be expected since duration of exposure is a key factor in the determination of carcinogenic risk, and the composite (lifetime) receptor is assumed to have adult characteristics for 50 years of their assumed lifetime (70 years). However, this does highlight the importance of assumptions related to the characteristics of each receptor group as well as assumptions related to time patters (duration of lifetime, length of time in Deloro). In terms of pathway contributions to variance, general food basket was by far the most significant contributor of variance to the composite ER value for arsenic. Drinking water, home garden produce, soil/dust ingestion, dermal exposure were lesser albeit significant contributors to the variance.

The PDF characterizing background intake of inorganic arsenic from food (general food basket) has the most significant influence on the overall model outcome for the adult component of the arsenic ER estimate. Parameters such as body weight, water consumption, and soil concentration also play important roles in the calculation of potential exposures arising from contaminant concentrations in the town. Similar results were noted for other receptors groups, exposure scenarios (non-home garden consumers) and locations (zones) [charts not shown].

Results for lead indicate that the PDF characterizing soil concentration is the most significant contributor to the variance within the ER estimates. Vegetable consumption, body weight, fruit consumption, and soil/dust ingestion also contribute significantly to the variance.

The results of the sensitivity analysis identify the variables to which the risk characterization is most sensitive. If low confidence is placed on a variable displaying a high sensitivity than the results of the assessment may be questionable and one would want to better define that variable. In the current assessment, however, the estimates of the model parameters to which the risk characterization was most sensitive were ones that were considered realistic and conservative in nature. As such, there is confidence that the Exposure Ratio results are accordingly realistic and conservative.

Several uncertainties have been identified throughout the course of the assessment. The following sections characterize where uncertainties have been identified and how the risk assessment was impacted.

6.1 Environmental Media Concentrations

- Inorganic arsenic exposure estimates for children *via* general food basket consumption reported by Environment Canada (1993) appeared to be quite high relative to other references (OMOEE, 1996; Yost *et al.*, 1998). The plausible maximum and 95th percentile exposure estimates to inorganic arsenic were most likely a result of the maximum inorganic arsenic exposure estimates *via* general background food basket. For some chemicals, age-specific exposure levels were not available, therefore exposure estimates (reported on a g/day basis) were divided by age-specific body weights, which would tend to significantly overestimate exposure, especially for infants whose diets would be considerably different and less likely to contain contaminants.

- In the consideration of indoor surface dust concentrations, it was concluded that there were too many uncertainties in using either swipe samples or the dustfall samples. Therefore, the indoor surface dust concentrations were estimated based on a outdoor soil/indoor dust relationship derived by Hwang *et al.* (1997) and Calabrese (unpublished). This was considered more scientifically sound, as the soil sampling programme was comprehensive, there were no concerns about use of data for samples with concentrations less than the detection limit, and estimated exposures would not be impacted by altered behaviours of residents cleaning house more thoroughly than normal (whether due to concerns regarding contamination or due to tidying prior to the sampling period).

- The proportion of inorganic arsenic present in vegetables has been reported to be approximately 5 to 10 percent (Pyles and Woolson, 1982; Weiler, 1987). However some uncertainty regarding the proportion of inorganic arsenic present in fruit has been observed. Several literature sources have indicated inorganic arsenic levels between 10 and 74 percent in fruit (OMOE, 1987; Weiler, 1987).

- Although indoor inhalation of air is a minor contributor to the overall exposure estimates, it should be noted that the concentrations in the majority of indoor air samples were less .than the detection limit. Hence, outdoor air concentrations were used to characterize indoor air, which would provide less certainty in comparison to using direct indoor air measurements.

- Uncertainties related to the sampling and analysis of chemical concentrations in the media of potential concern may also impact the risk assessment. It was assumed that the data supplied for the risk assessment were representative of concentrations in Deloro, although it is possible that the methodologies employed might over- or underestimate the site conditions. Also related to analysis is the uncertainty regarding

the "actual" concentration of a chemical for which analysis indicates a concentration below detection. Theoretically, the value of that concentration could be any value between zero and the detection limit. While the most conservative value to use in the assessment would be the detection limit itself, it was considered to be realistically conservative to employ a value of one-half the detection limit when the exposure concentration was listed as below the level of detection.

- Chemical concentrations at the site were assumed to remain unchanged in the future. However, as the former mine site is the suspected source of dusts which are responsible for contamination of environmental media in Deloro village, it is likely that mitigation of the chemical concentrations on the former mine site would result in decreased levels of chemicals in the village over time.

6.2 Exposure Assessment

- Uncertainty in the estimation of exposure in risk assessment is generally related to a lack of specific knowledge about the site itself, the receptors of concern, or the scenarios in which those receptors may be exposed. In order to address these data gaps, data from the literature was employed as a basis for scientific judgement of values which would represent the realistic exposures. This approach was used in cases where data were lacking.

- The individual variability in physiological and behavioural parameters may be a source of uncertainty in risk assessment. Where site-specific data were lacking, receptors and their characteristics were selected in an attempt to purposely overestimate potential exposures. An example of this might be soil ingestion by children; while there were no site-specific data describing soil ingestion, or activities leading to soil ingestion, data from the U.S. EPA were employed. These data were considered comprehensive and conservative; as they were based on fecal soil content, soil ingestion from all sources was included, and it is unlikely that this value would underestimate typical soil ingestion.

- The bioavailabilities of chemicals are affected by the media through which exposure occurs. This issue was examined in some detail for arsenic, for example, and it was observed that exposure to particulate-borne arsenic were much lower than that for soluble arsenic in water. There were little data for determinations of such differences in bioavailability for other chemicals of concern, and even for arsenic, there were limited data regarding the bioavailability of arsenic in food. This lack of data was addressed through conservative estimates of bioavailability, for example, using 90% bioavailability for food-borne arsenic, in order to estimate exposures in a conservative manner. There were also some uncertainties regarding the oral bioavailability of arsenic in soil and dust. Although a default value of 80% has been used for arsenic by the U.S. EPA, the published literature indicated maximum bioavailabilities of arsenic in soil and dust of 14 and 19%, respectively (Freeman *et al.*, 1993, 1995). These values were considered realistic, based not only on the published literature, but on

site-specific data which indicates that arsenic in Deloro soils is in a less bioavailable form, based on their relatively low uptake into plants. This reduction in bioavailability of soil-borne arsenic may be related to the chemical form in Deloro soils, or may be due to interactions of arsenic with components of the soil. Being less bioavailable to plants supports the likelihood that there would be relatively low bioavailability in the gut as well. Thus the use of the Freeman *et al.* data was considered realistic, and not likely to result in underestimation of exposure.

- Although the activities of most residents have been characterized by one or more of the exposure scenarios developed, a high level of uncertainty is associated with the amount of time a receptor may spend on the abandoned mine site and to what extent the receptors may contact the areas of extreme contamination. In addition, the actual activities associated with the more sensitive receptors (*i.e.*, preschool children and children) while on the mine site are not certain. Hence, exposure estimates for this scenario were based primarily on assumptions designed to provide a conservative estimate of exposure.

- Infants were assumed to have the same soil ingestion as preschoolers. This is a very conservative soil ingestion estimate, considering that an infant (0 to 6 months) would most likely not have the same accessibility to soil as a preschooler (6 months to 4 years), given differences in mobility between these age classes. In addition, the amount of skin available for dermal contact has also been conservatively estimated. Generally, one would not expect an infant to have a significant amount of skin exposed for dermal contact with soil and dust.

- Dermal contact for metals is generally a very minimal pathway of exposure, as seen in this assessment for lead, nickel, cobalt and silver. In comparison, the dermal exposure to arsenic comprised a more significant pathway. This may be due to a series of conservative assumptions, such as dermal adherence factors and exposed surface area, as well as dermal bioavailability. Just as dermal exposure was more significant for arsenic, so was the dermal bioavailability higher than that for other metals. In addition, the more conservative estimate of dermal bioavailability of arsenic was used in the assessment, although this value (1.8%) was for absorption of arsenic in an aqueous matrix, whereas the lower value (0.9%) would have been more relevant to exposures in Deloro as it was based on exposure to arsenic in a soil matrix.

- Garden test plots were not located in areas associated with the entire range of concentrations characteristic of Deloro (*i.e.*, the mean arsenic concentrations for the town of Deloro was much greater then that found in the garden test plots). Therefore, site specific biotransfer factors (BTFs) were used in an attempt to capture elevated soil concentrations and hence potentially elevated fruit and vegetable concentrations. Although using site-specific BTFs is a more conservative approach than using the available test plot data, a level of uncertainty is produced by using such transfer factors. Specifically, uncertainty is based on the lack of knowledge regarding the actual range of concentration in all gardens in Deloro, and whether BTFs in the lower

concentration range would hold true for elevated concentrations. For example, the range of soil concentrations of lead in garden or backyard (where a garden might be located in future) was much lower (maximum 250 mg/kg in gardens versus 605 mg/kg for the whole town). This would be indicative that the upper range of exposures to lead through home garden produce would have been overestimated.

- With the exception of arsenic, the same site-specific BTFs (which were derived from the phytotoxicology report data) were applied to fruits (*i.e.*, apples, pears, peaches, *etc.*). This may be an overestimate of actual fruit specific BTFs, given that data in the published literature would suggest that fruits accumulate lower concentrations of certain metals than do vegetables.

- Some uncertainty was associated with the actual amount of home grown produce a family could consume. For the current assessment, it was conservatively assumed that a family of four would consume 100% of the total garden yield. In addition to this assumption, annual backyard garden yields were based on an assumed garden size and an estimated average crop yield. Depending on the actual family size, garden size, and crop yield, this may be an over- or underestimate of individual exposure. However, given that there was no reduction of exposures to home garden produce due to crop loss (*e.g.*, wildlife browsing or spoilage), it is concluded that the estimates employed in this assessment would be conservative.

6.3 Hazard Assessment

- In the derivation of limits by regulatory agencies, large uncertainty factors (*i.e.*, 100-fold or greater) were used in the estimation of the reference dose (RfD) for threshold-type chemicals. These safety factors were applied to exposure levels from studies where no adverse effects are observed (*i.e.*, to the NOAEL). Thus, exceeding the toxicological criterion does not mean that adverse effects would occur. Exposures greater than the calculated toxicological criterion may also be without risk (*i.e.*, below the threshold for adverse effects in humans), but this could not be, or was not, determined by the agency which derived the toxicological criterion.

- Humans were assumed to be the most sensitive species with respect to toxic effects of chemical. However, for obvious reasons, toxicity assays are not generally conducted on humans, so toxicological data from the most sensitive laboratory species were used in the estimation of toxicological criteria for humans.

- In comparing the risks to Deloro residents to those for typical Ontario residents, the assumption was made that there are no particular sensitivities or predispositions of Deloro residents to the toxicity of any of the chemicals of concern. Based on the health studies of the village conducted by Goss-Gilroy and by the Medical Officer of Health for the region, and based on site characterization data, this is considered a reasonable assumption, and would not affect the conclusions of the risk assessment.

- For genotoxic carcinogens, it was assumed that no repair of genetic lesions occurs, and that, therefore, no threshold can exist for chemicals that produce self-replicating lesions. However, the existence of enzymes that routinely repair damage to DNA are well documented in the scientific literature, and the potential adverse effects arising from damage to DNA would only be observed if the ability of these repair enzymes to "fix" the damage was exceeded.

- In the case of arsenic, there is agreement in the published literature that the methods used to estimate the oral toxic potency of arsenic based on exposures of Taiwanese populations to arsenic in drinking water would significantly overestimate cancer risks at lower levels of exposures, such as that experienced by the general North American population. The use of such data would thus result in an overestimation of cancer risk for the populations of Deloro and Ontario.

- Recently, there has been concern on the part of regulators regarding the applicability of the arsenic cancer potency estimates for cancers at other sites (specifically bladder cancer) in setting exposure limits for arsenic. The National Research Council (NRC, 1999) has recently re-evaluated drinking water criteria for the United States, based on bladder cancer incidence data in the Taiwanese population as presented in Wu *et al.* (1989), Chen *et al.* (1992) and Smith *et al.* (1992). NRC (1999) emphasized that the evaluation of cancer potency factors for bladder cancer has been limited by the amount and the quality of data available for use in the linear model. While the bladder cancer value would yield a greater cancer potency than that based on skin cancer, these data are still limited by many of the same problems as the potency factor for skin cancer, including large uncertainty of total daily exposure to inorganic arsenic (*i.e.,* the poor linkage between water concentrations of arsenic and individual exposure, and lack of data on arsenic intake from food), concomitant exposures to other chemicals and carcinogens (which would be especially important if arsenic is a cancer promoter), and differences in nutritional and health status between Taiwanese and North American populations. The impact on the results of this risk assessment is considered to be negligible, as the primary benchmark for evaluation of risks to Deloro residents were the risks estimated for typical Ontario residents. The risk assessment for Deloro and Ontario residents employed the same methodologies, the same assumptions and used the same exposure limit. Therefore, because risks to Deloro residents were not significantly elevated in comparison to Ontario residents, Deloro residents were not considered to have unacceptable risks.

- In addition, the basis for the inhalation cancer potency factor for arsenic was an air concentration derived from occupational epidemiological studies. It has been suggested that because exposures to air-borne arsenic would be mediated by inhalation of particulate matter, and since a higher proportion of particulate matter would be respirable in occupational settings as compared to environmental exposures, the inhalation potency of arsenic is likely overestimated for exposures associated with environmental contamination.

6.4 Urinary Arsenic Uncertainties

- The measurement of speciated urinary arsenic is considered the most reliable method for estimation of recent daily exposure to inorganic arsenic; however, there is some evidence in the published literature that indicates that the consumption of forms of arsenic found in seafood (arsenobetaine, arsenocholine, arsenosugars, *etc.*) may increase the urinary concentration of speciated arsenic. This could lead to overestimation of the daily exposure to inorganic arsenic for seafood consumers. This is considered to have limited impact on the risk assessment for Deloro residents, however, as it is considered likely that the dietary content of the seafoods with which this phenomenon has specifically been observed (*i.e.*, marine fish, kelp and bivalves) is relatively small for Deloro residents. Further, the good agreement between the estimated urinary speciated arsenic concentrations (based on the identified exposure pathways, not including seafood consumption) and the actual urinary concentrations supports the validity of the measure of urinary speciated arsenic as a reliable indicator of recent exposure to inorganic arsenic.

- There was a large number of speciated urinary arsenic samples (taken from Deloro) which had concentrations less than the detection (*i.e.*, below 6 μg/L), which can be considered to be a source of uncertainty in the characterization of exposure and risk. While this limitation would not alter the conclusions of the urinary arsenic evaluation with regard to risks, it introduces a measure of uncertainty in the validation of the urinary arsenic model.

- Uncertainty exists with regard to actual daily urinary arsenic volumes of individuals. The current assessment employed data from various literature sources to characterize the urine output of individuals in Deloro, however specific volumes were not known and thus creates a level of uncertainty.

- Human receptors and their characteristics were selected in an attempt to estimate potential exposures in a reasonable yet conservative manner. There was a slight overestimation of urinary arsenic concentrations by the urinary arsenic model, which suggests that the exposure assessment modelling was based on conservative values and assumptions. This implied conservatism may be due to the overestimation of exposures associated with typical behaviours, but may also reflect alteration of behaviour in citizens who have responded to concerns over contamination in their village by minimizing exposure to contaminated media. Since the urinary arsenic model relied on the same exposure model as was used in estimating risks from exposure to arsenic, it is reasonable to conclude that the characterization of potential health risks from exposure to arsenic was also conservative. The good agreement between the urinary arsenic monitoring and the results of the risk assessment supports the conclusion that the residents of Deloro are not being subjected to measurably increased risk of cancer in comparison to the rest of Ontario.

Given the above, this risk assessment may overestimate actual risks by a considerable degree, but will not underestimate potential health risks. However, due to the relatively large database of site specific information and the comprehensive nature of the probabilistic component of this assessment, this overestimation is not expected to be unduly unrealistic.

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FIGURE 5-1 RISK ASSESSMENT PARADIGM

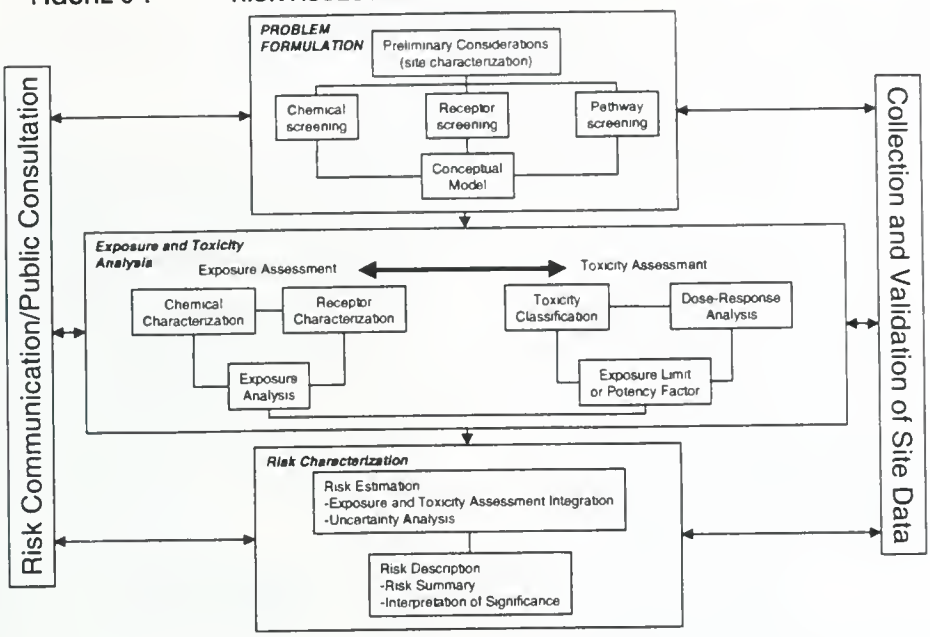


FIGURE 5-2 CONCEPTUAL MODEL - PROBLEM FORMULATION

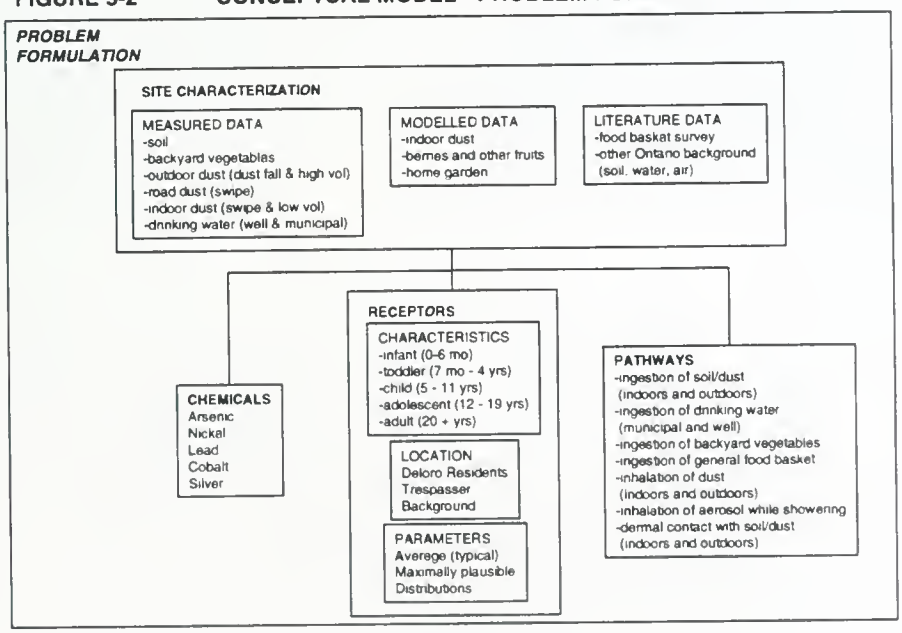


FIGURE 5-3 CONCEPTUAL MODEL - EXPOSURE, TOXICITY AND RISK

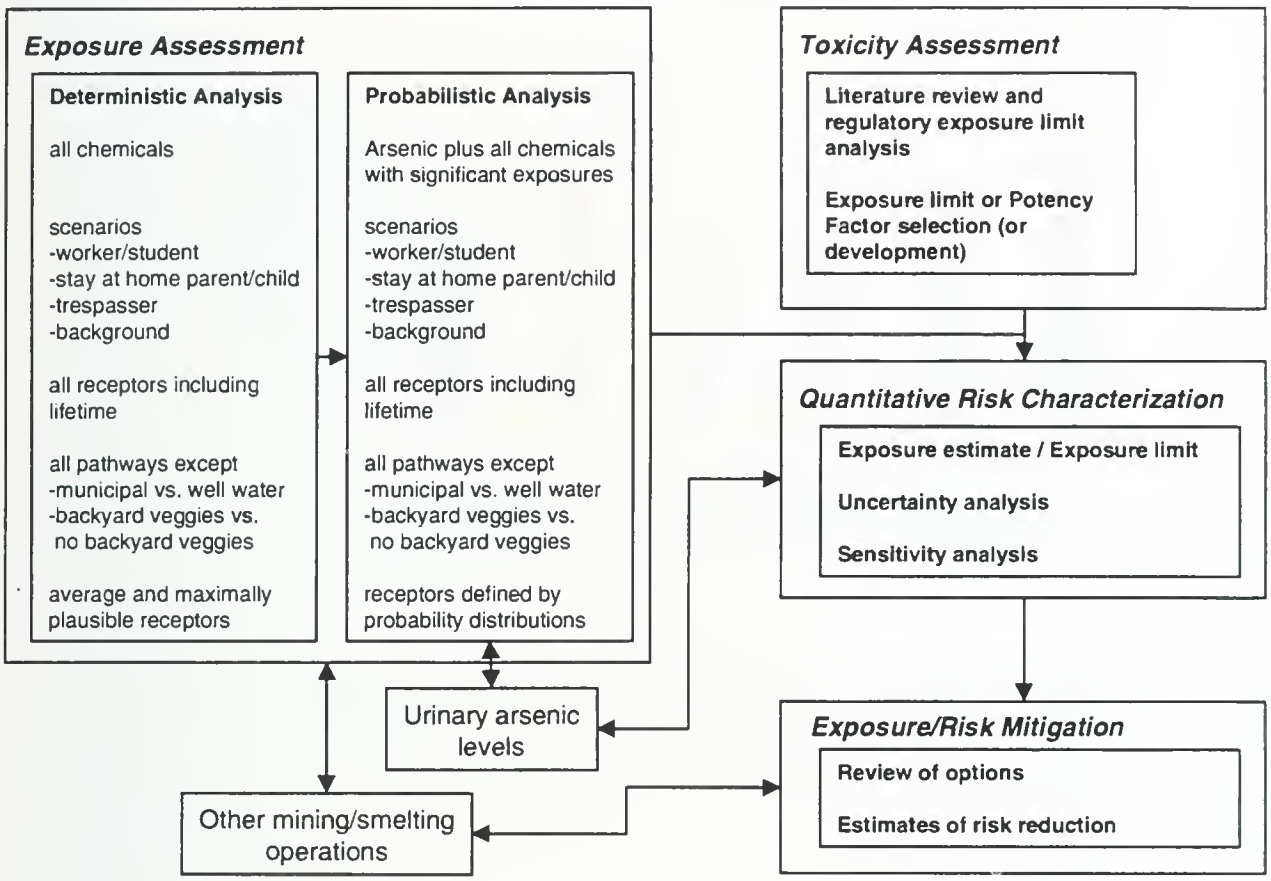


Figure 5-4
Estimated Lifetime Cancer Risk Levels (Deterministic)
Arsenic (all cancers)-home garden consumers

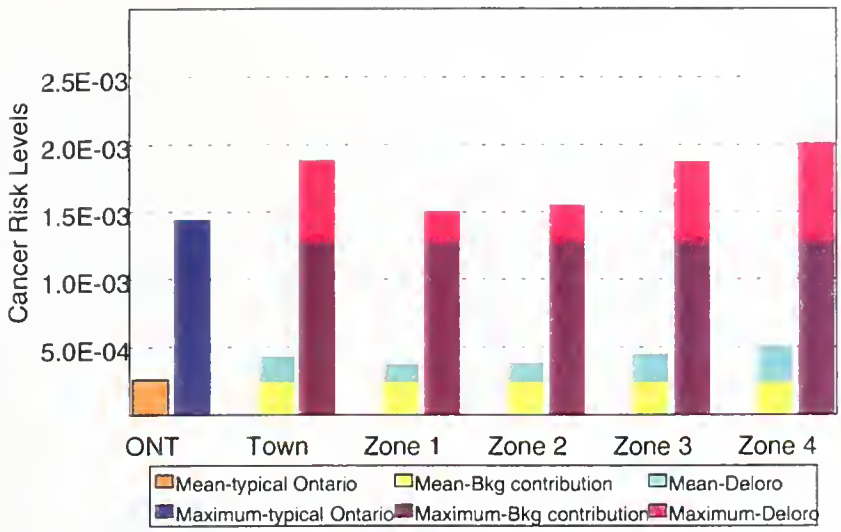


Figure 5-5
Estimated Lifetime Cancer Risk Levels (Deterministic)
Arsenic (all cancers)-non home garden consumers

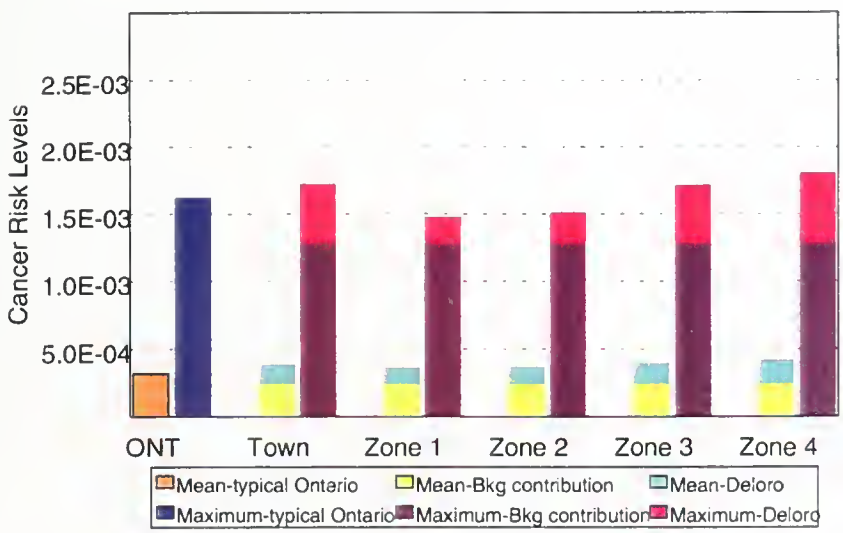


Figure 5-6
Incremental Estimated Lifetime Cancer Risk Levels (Deterministi
Arsenic (all cancers)-WHOLE TOWN

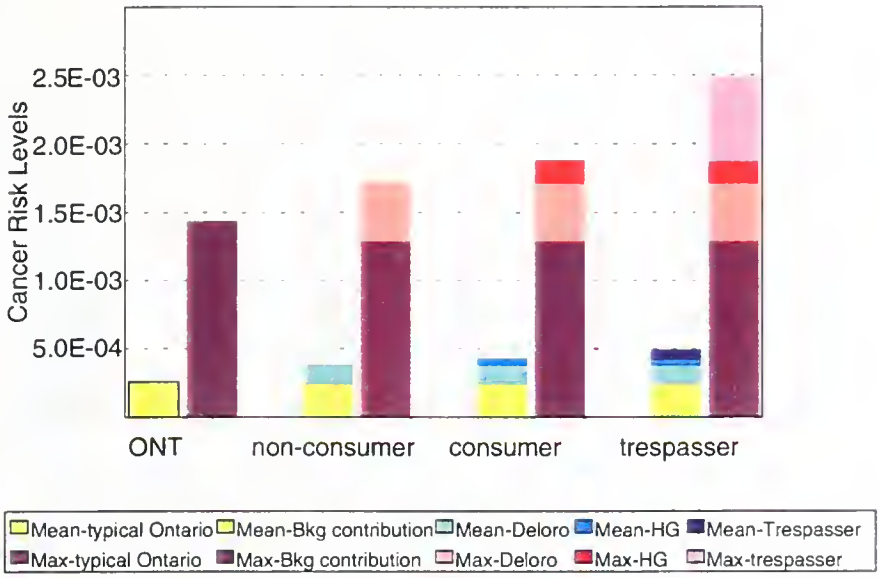


Figure 5-7
Long-term Exposure Ratios (Deterministic)
Arsenic (non-carcinogenic)-home garden consumers

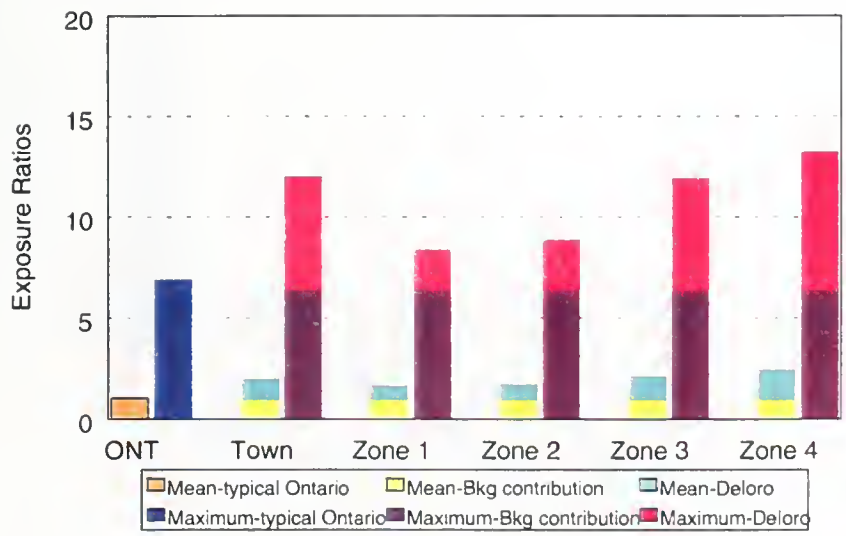


Figure 5-8
Long-term Exposure Ratios (Deterministic)
Arsenic (non-carcinogenic)-non home garden consumers

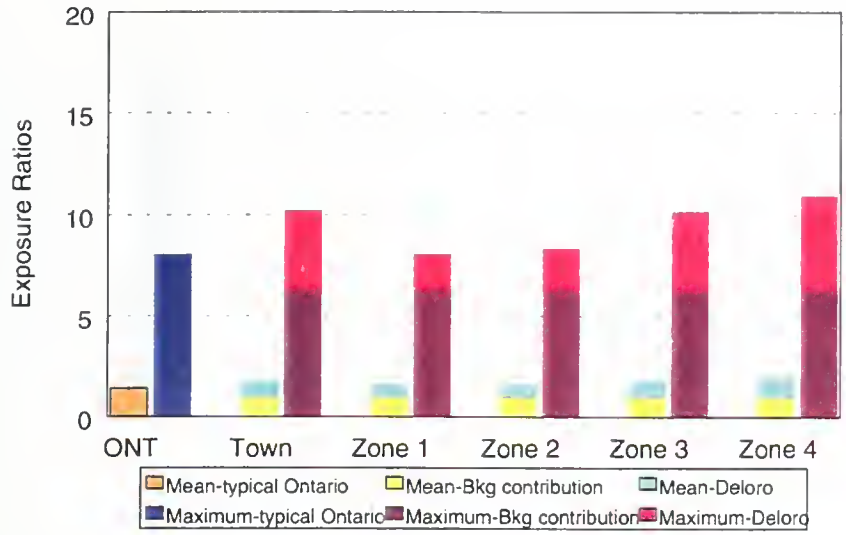


Figure 5-9
Long-term Exposure Ratios (Deterministic)
Cobalt-home garden consumers

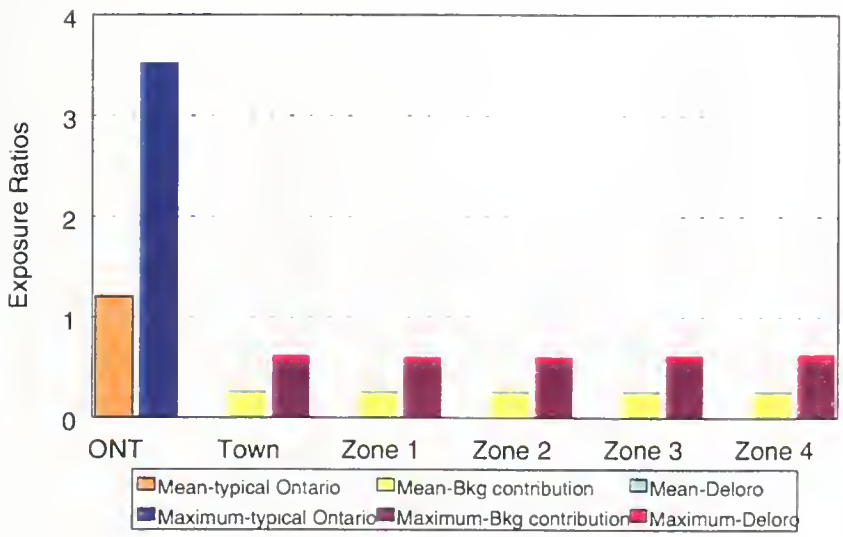


Figure 5-10
Long-term Exposure Ratios (Deterministic)
Cobalt-non home garden consumers

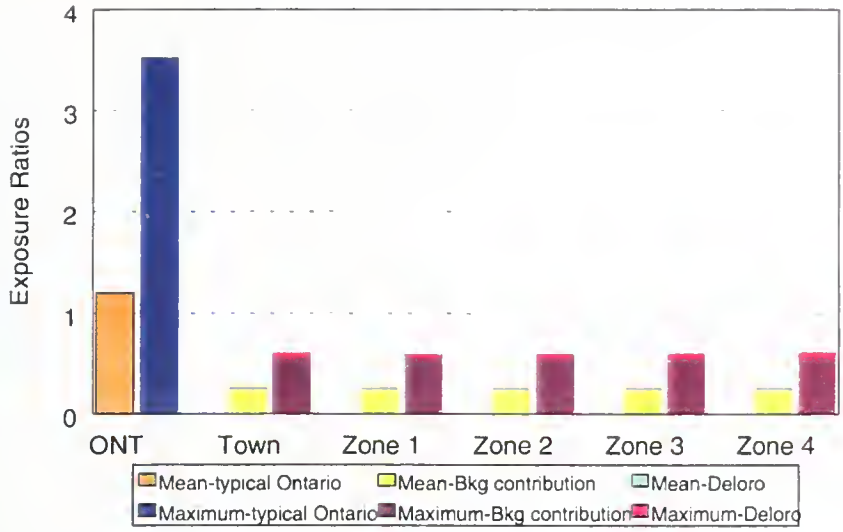


Figure 5-11
Long-term Exposure Ratios (Deterministic)
Lead-home garden consumers

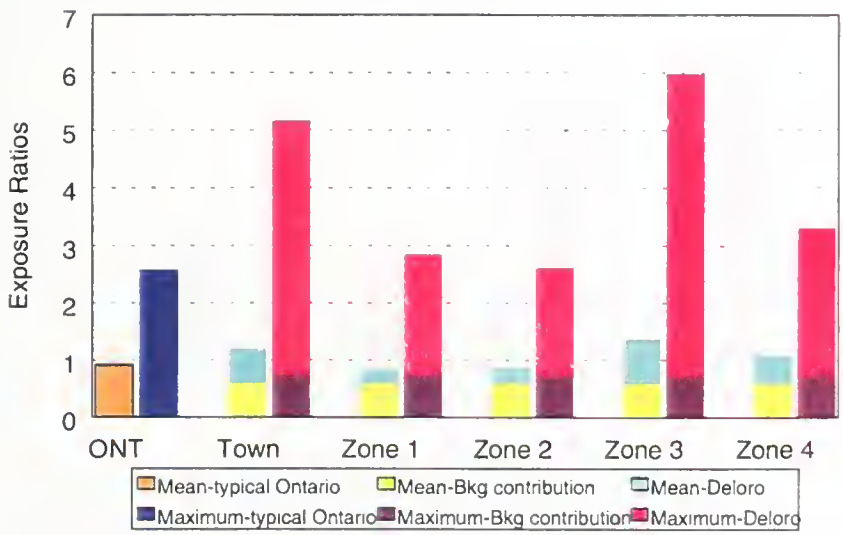


Figure 5-12
Long-term Exposure Ratios (Deterministic)
Lead-non home garden consumers

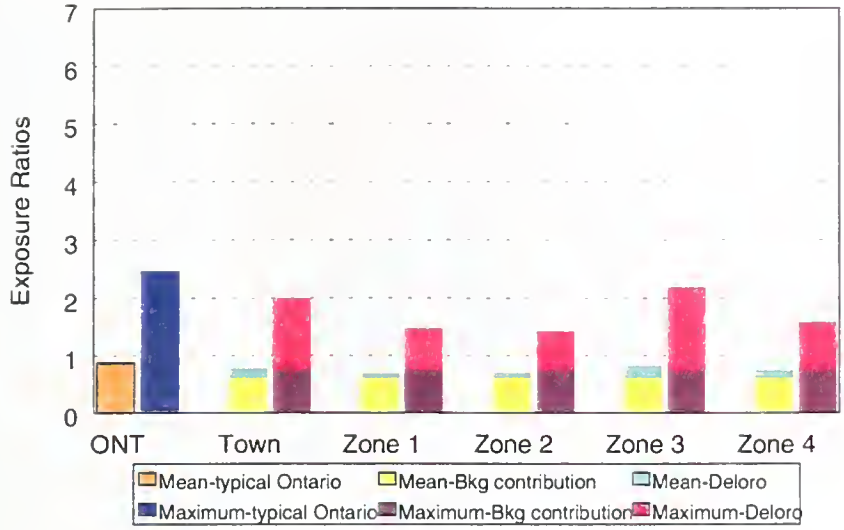


Figure 5-13
Incremental Long-term Exposure Ratios (Deterministic)
Lead-WHOLE TOWN

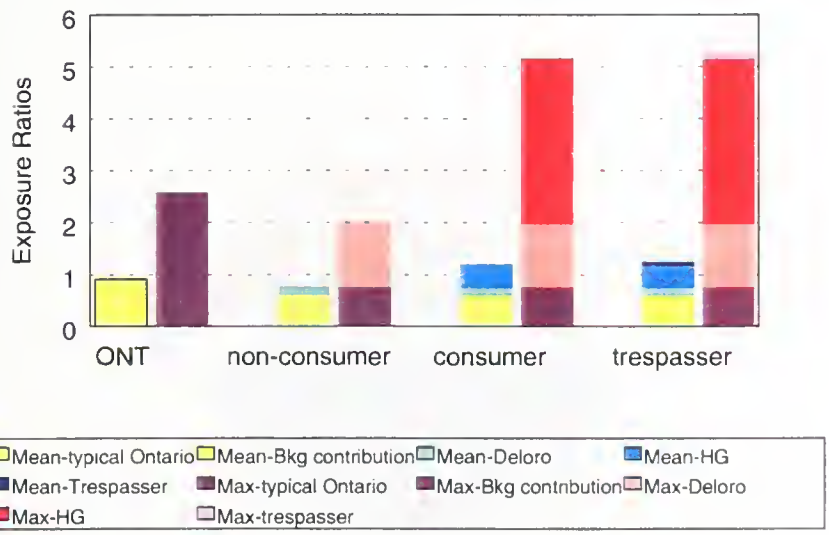
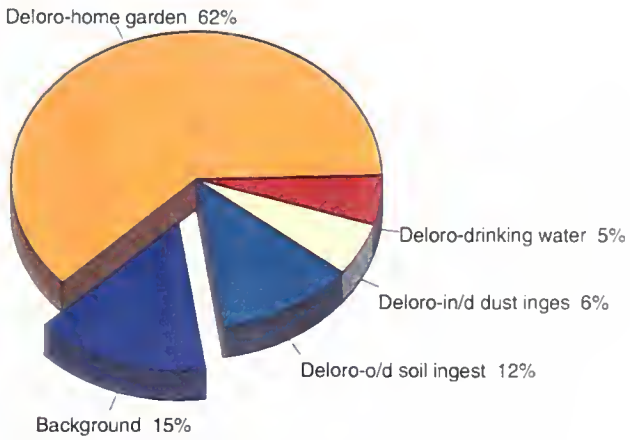
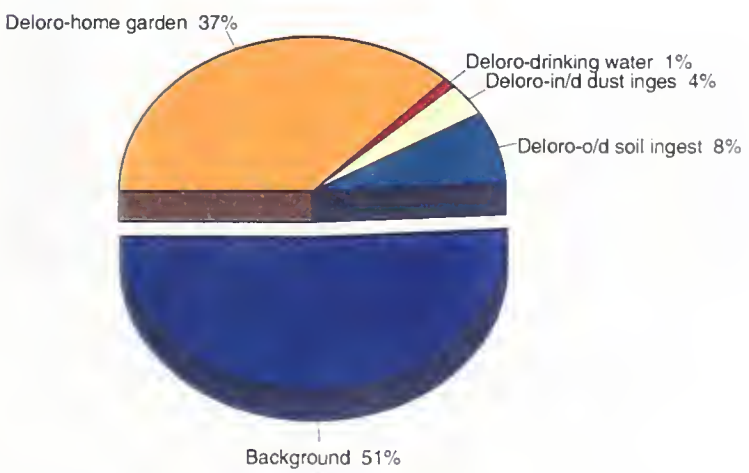


Figure 5-14
Exposure Pathways Analysis (% of Risk) - Lead
[maximum preschool child home garden consumer]



pathways contnbuting to greater than 1% of the overall nsk (ER) are included

Figure 5-15
Exposure Pathways Analysis (% of Risk) - Lead
[mean preschool child home garden consumer]



pathways contnbuting to greater than 1% of the overall nsk (ER) are included

Figure 5-16
Long-term Exposure Ratios (Deterministic)
Nickel-home garden consumers

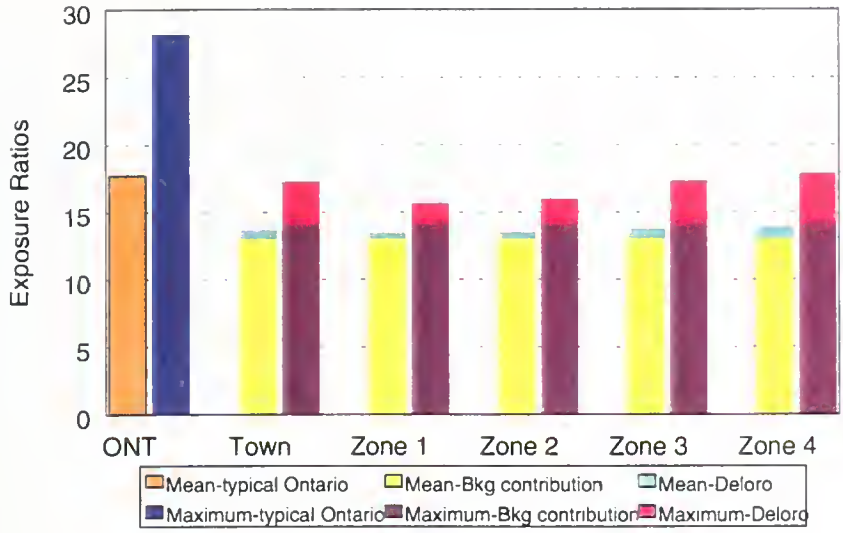


Figure 5-17
Long-term Exposure Ratios (Deterministic)
Nickel-non home garden consumers

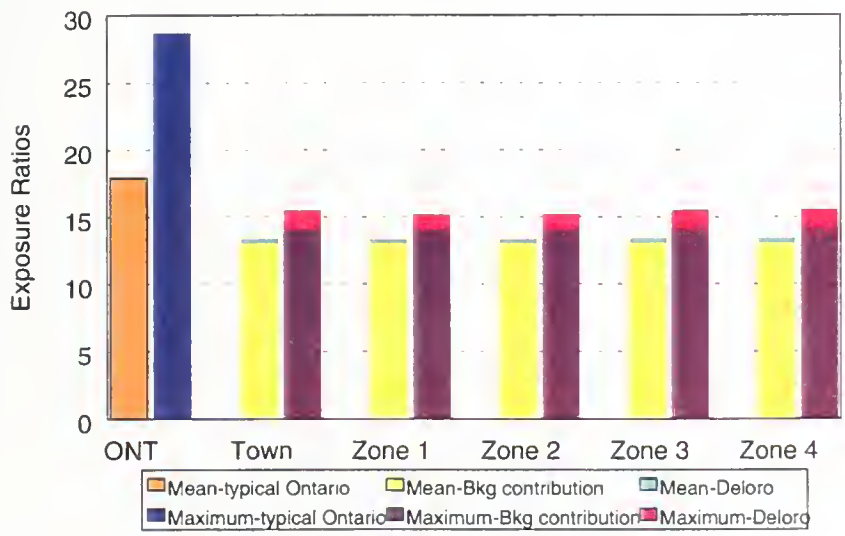


Figure 5-18
Long-term Exposure Ratios (Deterministic)
Silver-home garden consumers

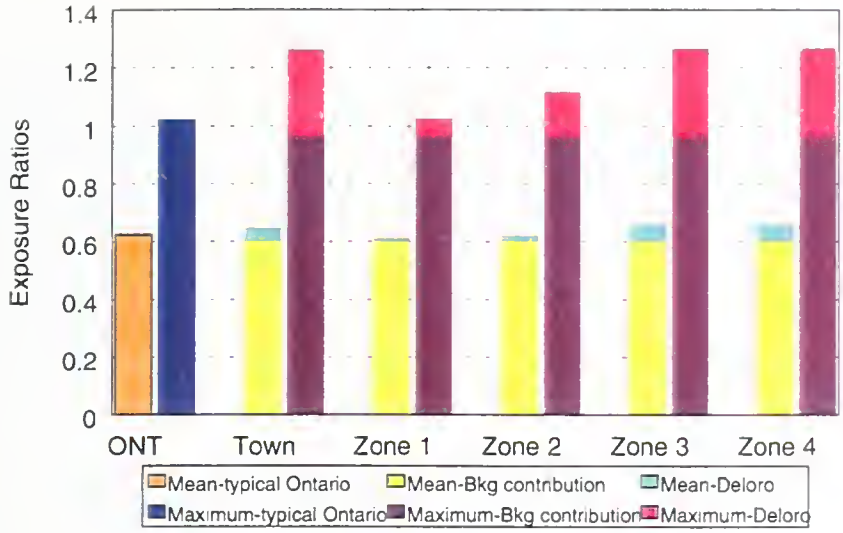


Figure 5-19
Long-term Exposure Ratios (Deterministic)
Silver-non home garden consumers

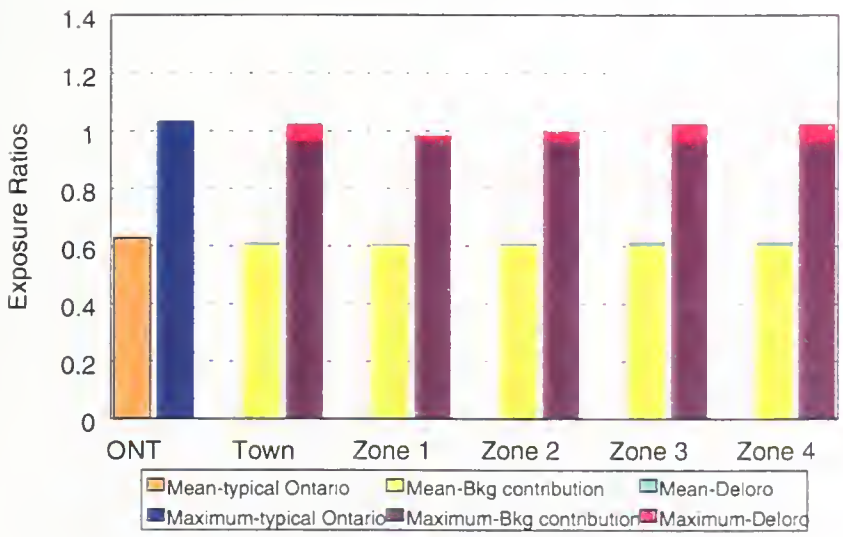


Figure 5-20
Estimated Lifetime Cancer Risk Levels (Deterministic)
Arsenic (all cancers)-trespasser scenario

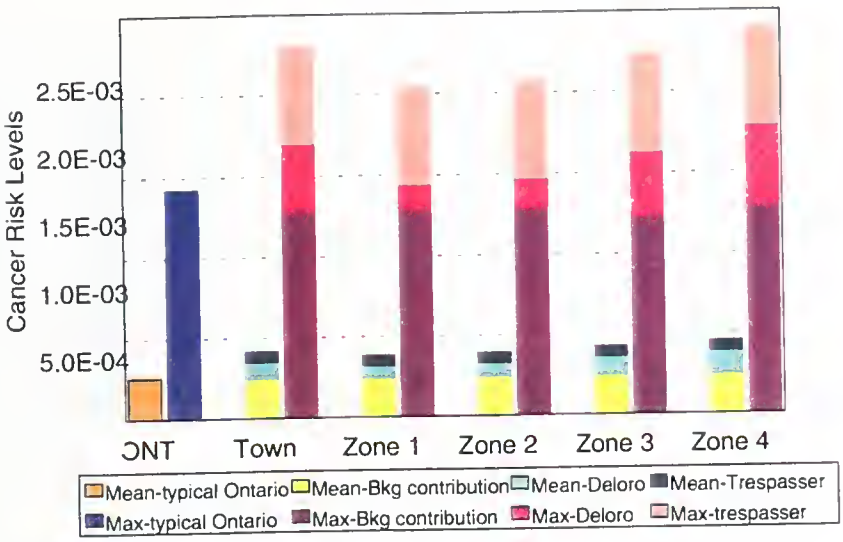


Figure 5-21
Long-term Exposure Ratios (Deterministic)
Arsenic (non-carcinogenic)-trespasser scenario

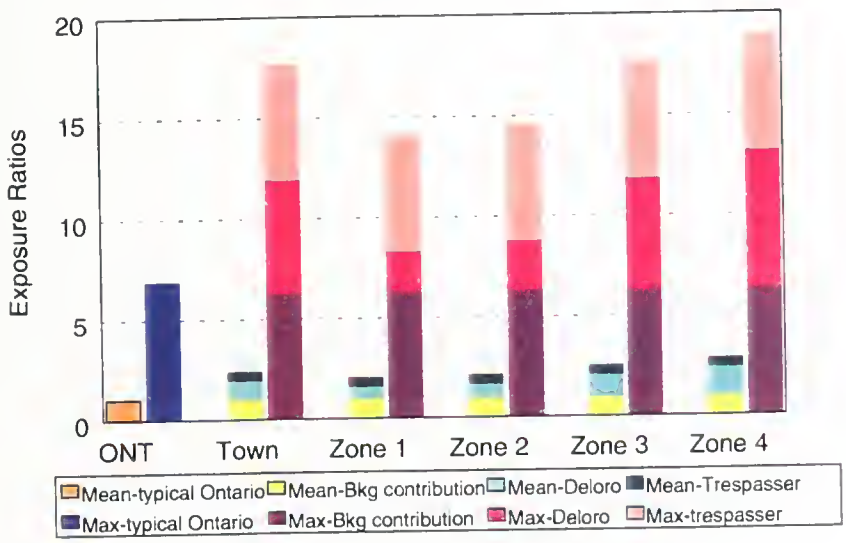


Figure 5-22
Long-term Exposure Ratios (Deterministic)
Cobalt-trespasser scenario

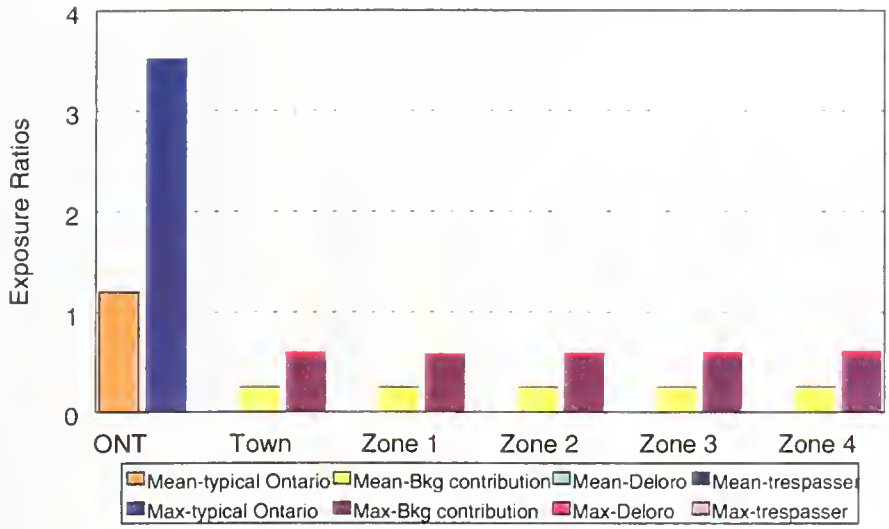


Figure 5-23
Long-term Exposure Ratios (Deterministic)
Lead-trespasser scenario

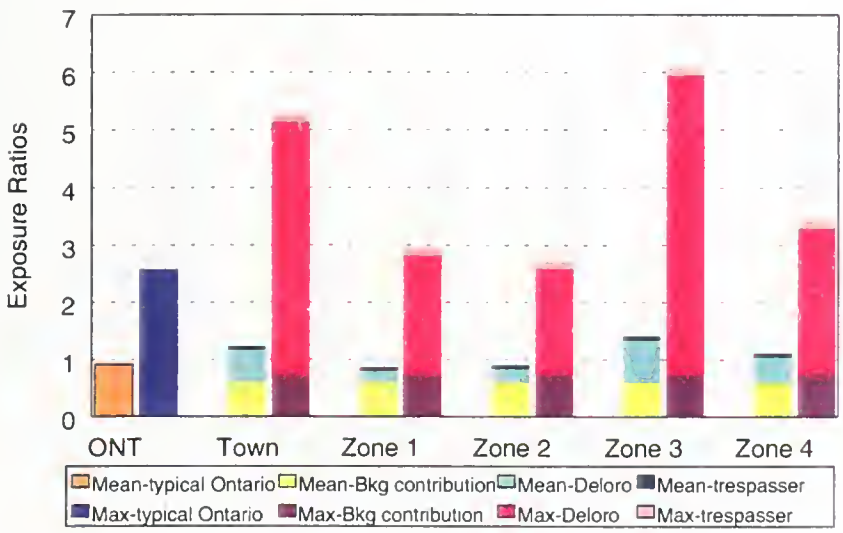


Figure 5-24
Long-term Exposure Ratios (Deterministic)
Nickel-trespasser scenario

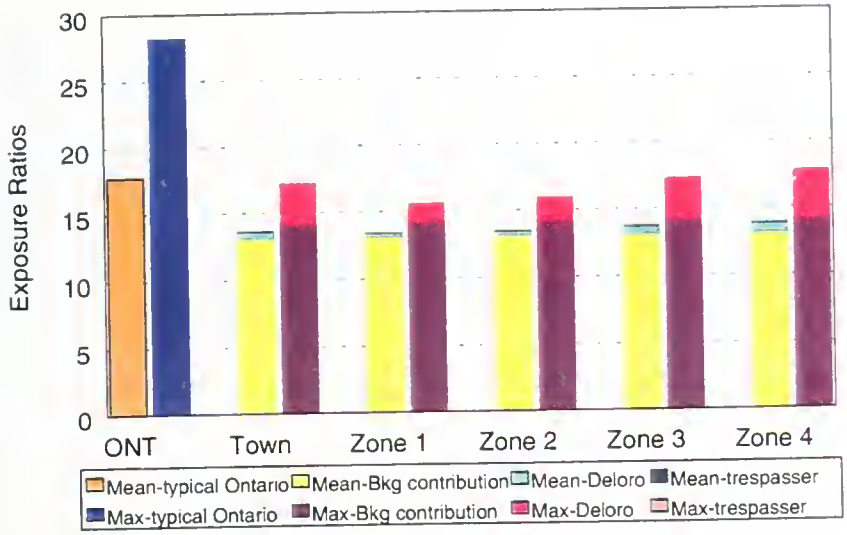


Figure 5-25
Long-term Exposure Ratios (Deterministic)
Silver-trespasser scenario

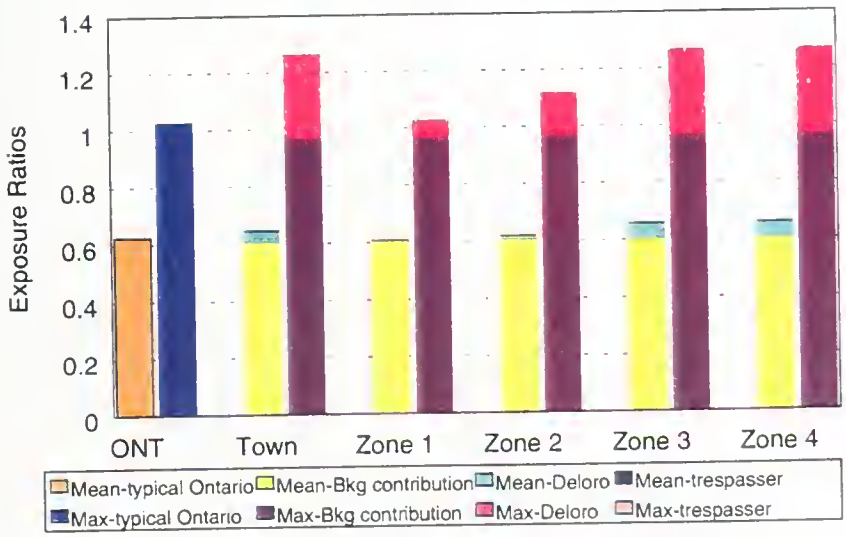


Figure 5-26
Estimated Lifetime Cancer Risk Levels (probabilistic)
Arsenic (all cancers)-home garden consumers

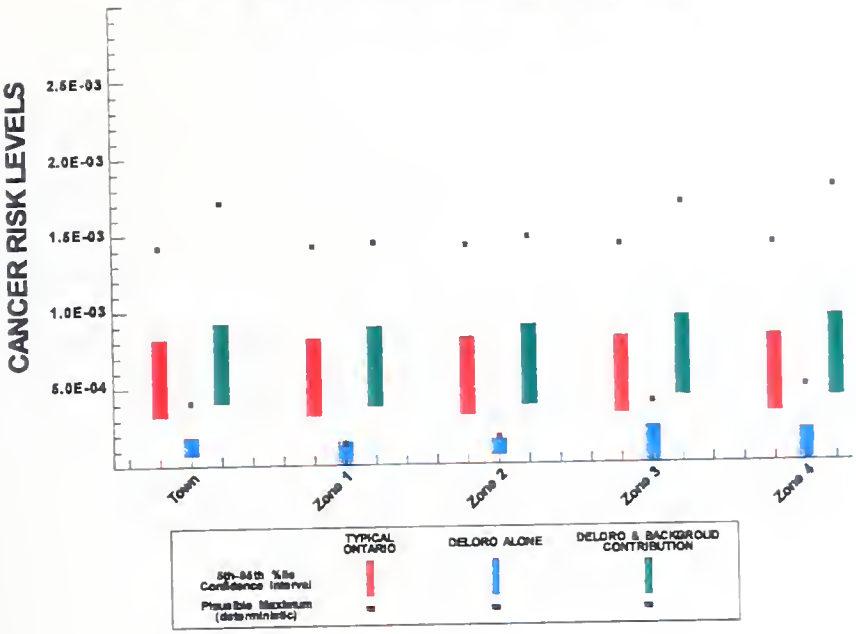


Figure 5-27
Estimated Lifetime Cancer Risk Level (probabilistic)
Arsenic (all cancers)-non home garden consumers

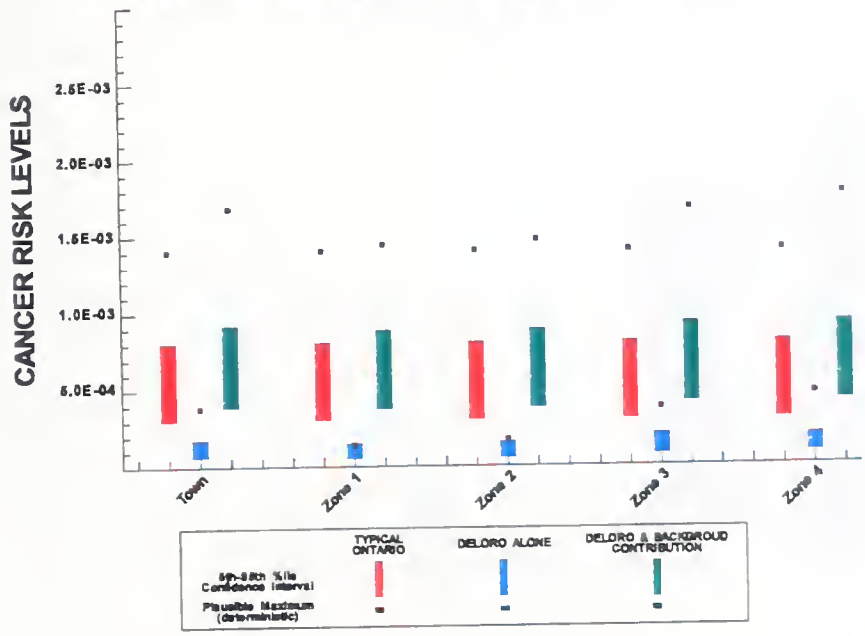


Figure 5-28
Incremental Lifetime Cancer Risk Levels (Probabilistic)
Arsenic (all cancers)-WHOLE TOWN

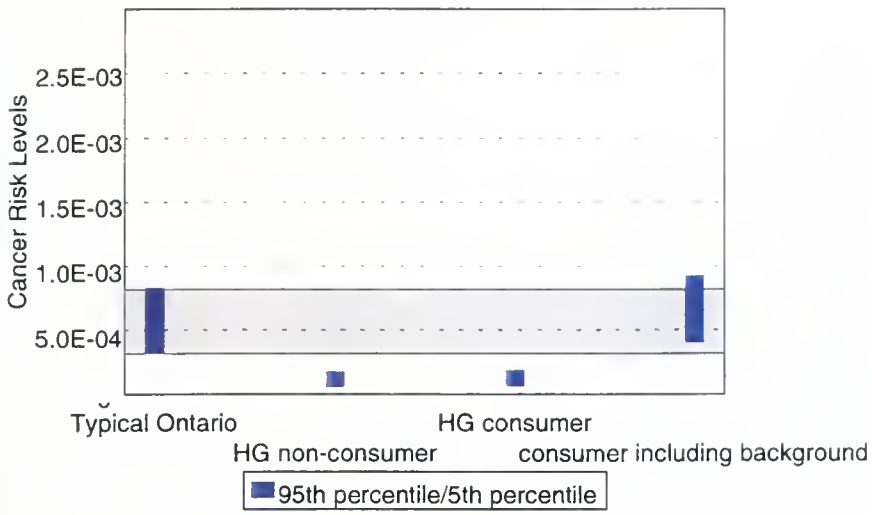


Figure 5-29 Contribution of Various Pathways to Preschool Child Receptor Exposure to Arsenic (Probabilistic Mean)

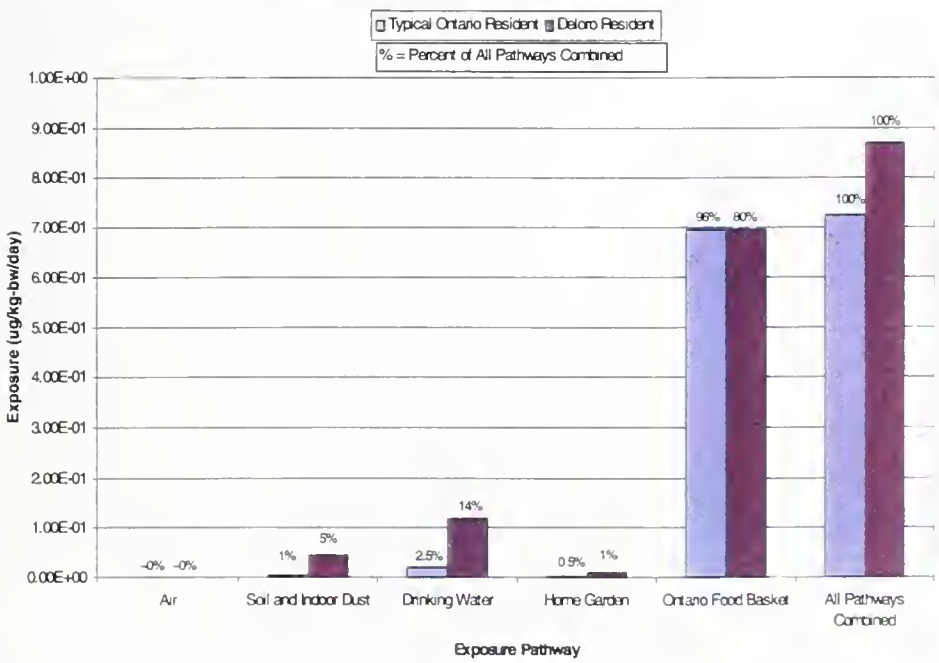


Figure 5-30 Contribution of Various Pathways to Adult Receptor Exposure to Arsenic (Probabilistic Mean)

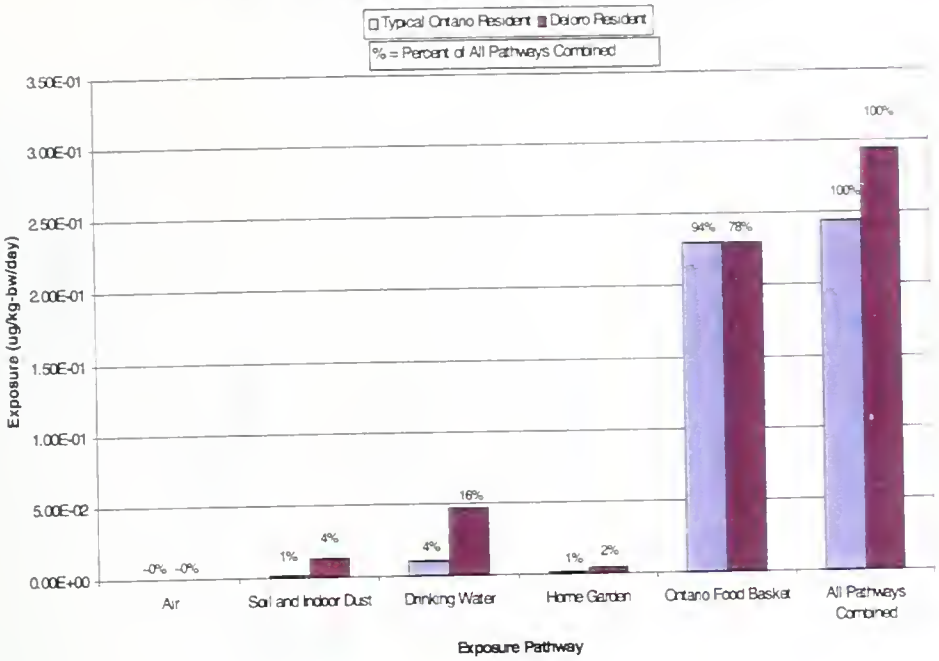


Figure 5-31 Contribution of Various Exposure Pathways to Lifetime Risk from Exposure to Arsenic (Probabilistic Mean)

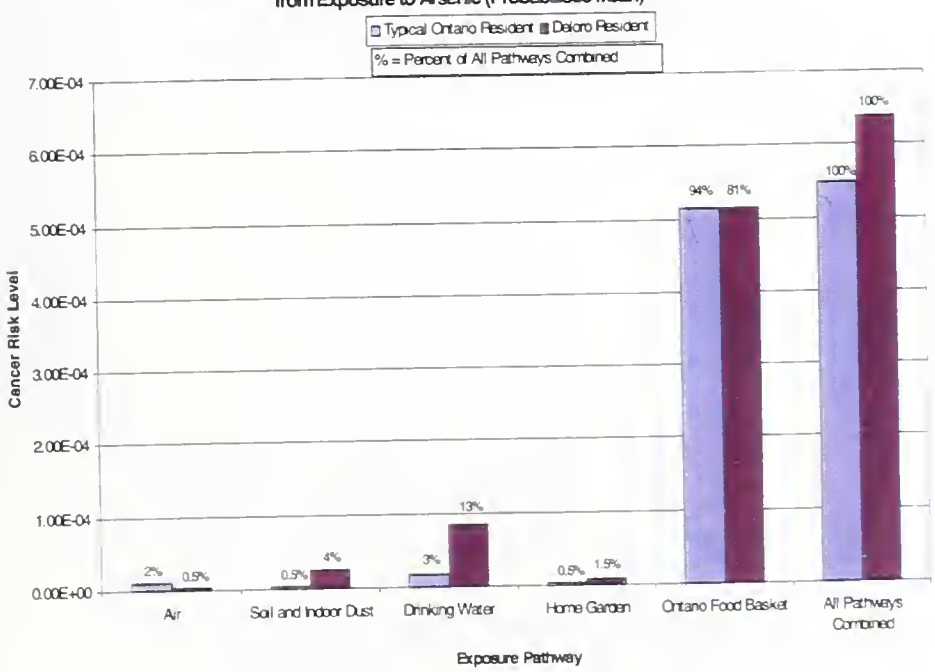


Figure 5-32
Long-term Exposure Ratio (probabilistic)
Arsenic (non-carcinogenic)-home garden consumers

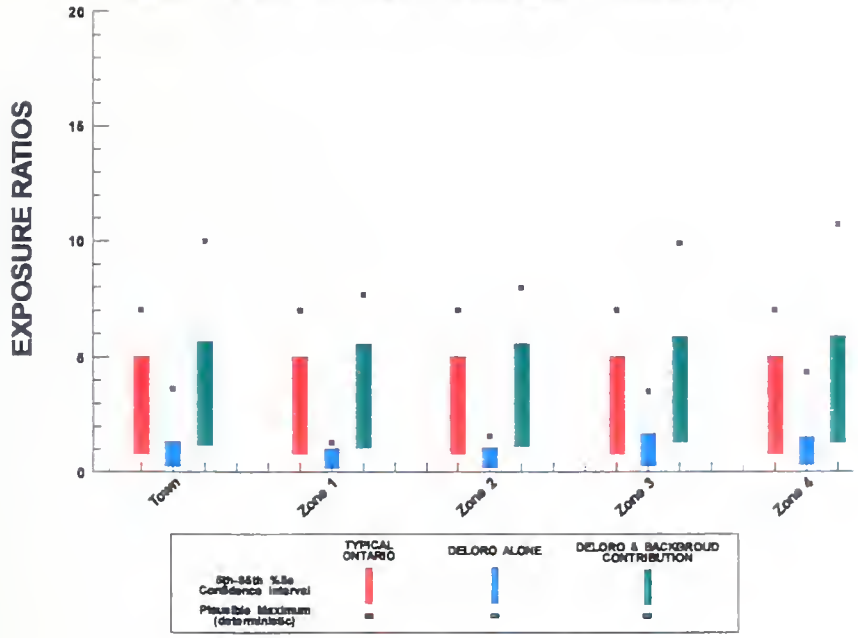


Figure 5-33
Long-term Exposure Ratio (probabilistic)
Arsenic (non carcinogenic)-non home garden consumers

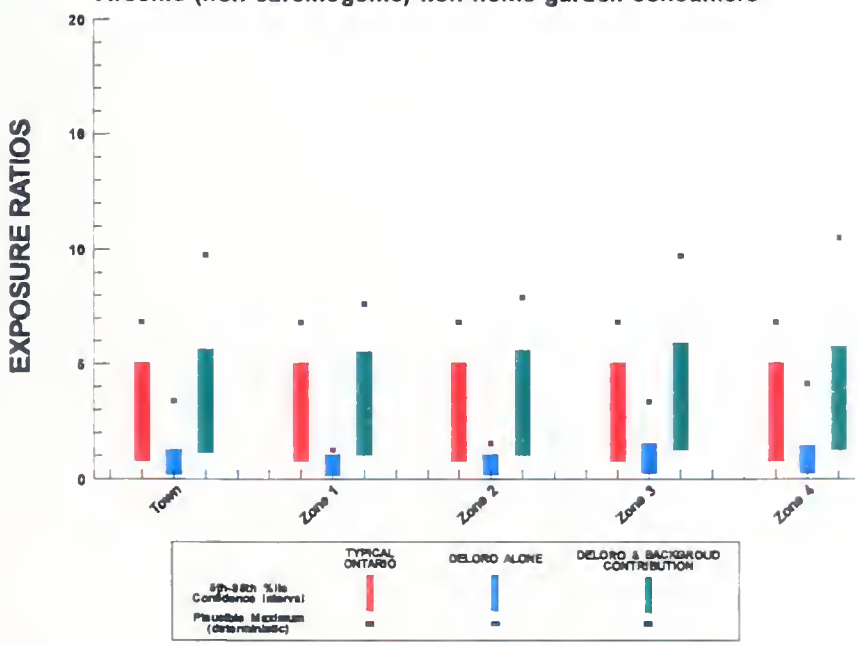


Figure 5-34
Long-term Exposure Ratio (probabilistic)
Lead-home garden consumers

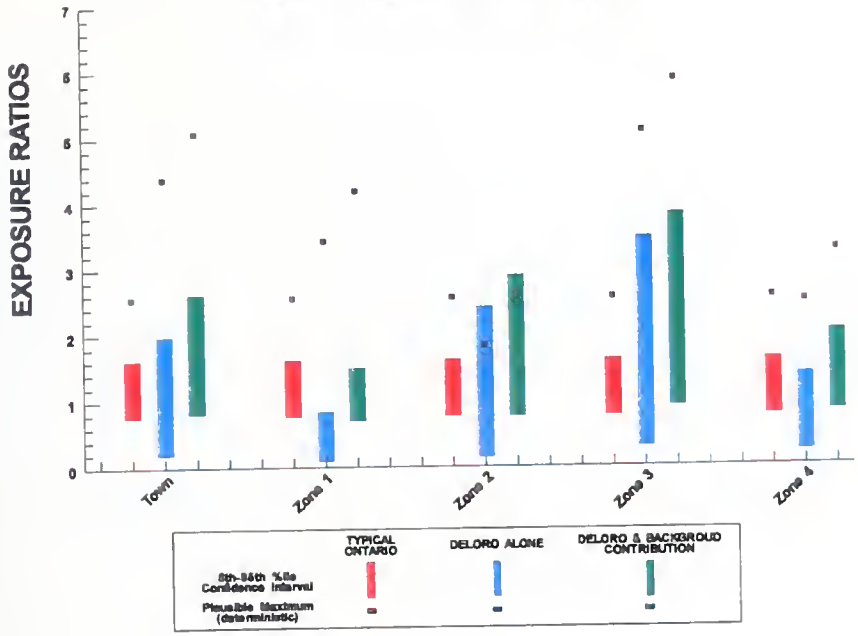


Figure 5-35
Long-term Exposure Ratio (probabilistic)
Lead-non home garden consumers

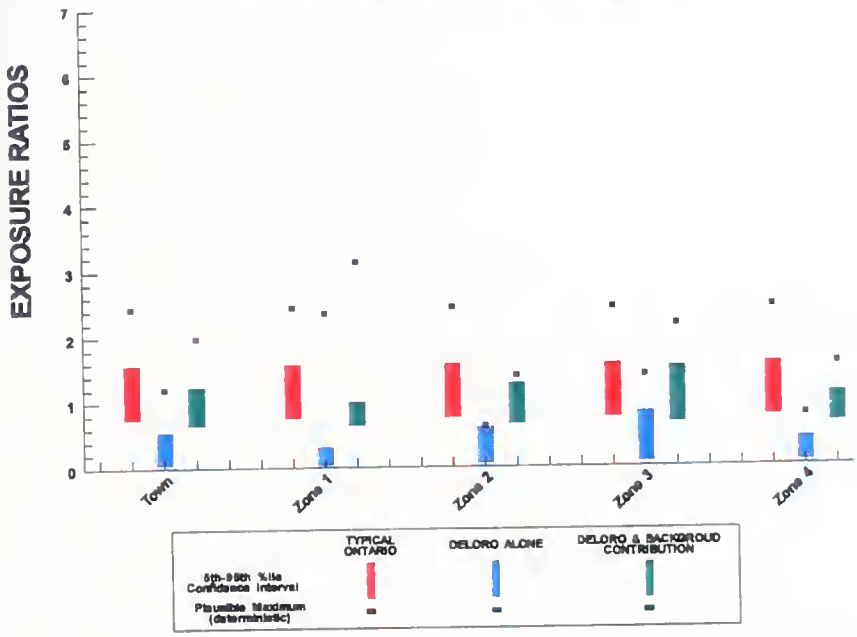


Figure 5-36
Incremental Long-term Exposure Ratios (Probabilistic)
Lead-WHOLE TOWN

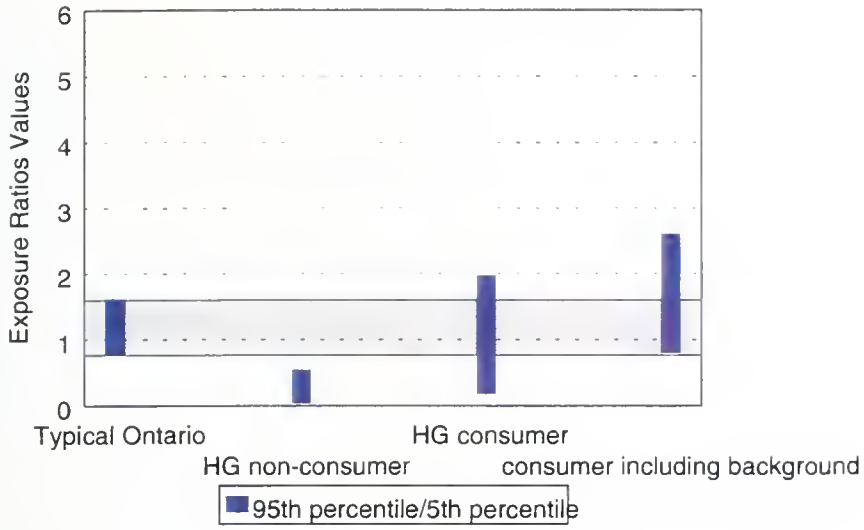


Figure 5-37
Speciated Urinary Arsenic Concentrations
Measured Data from Deloro Village, Havelock and Other Areas

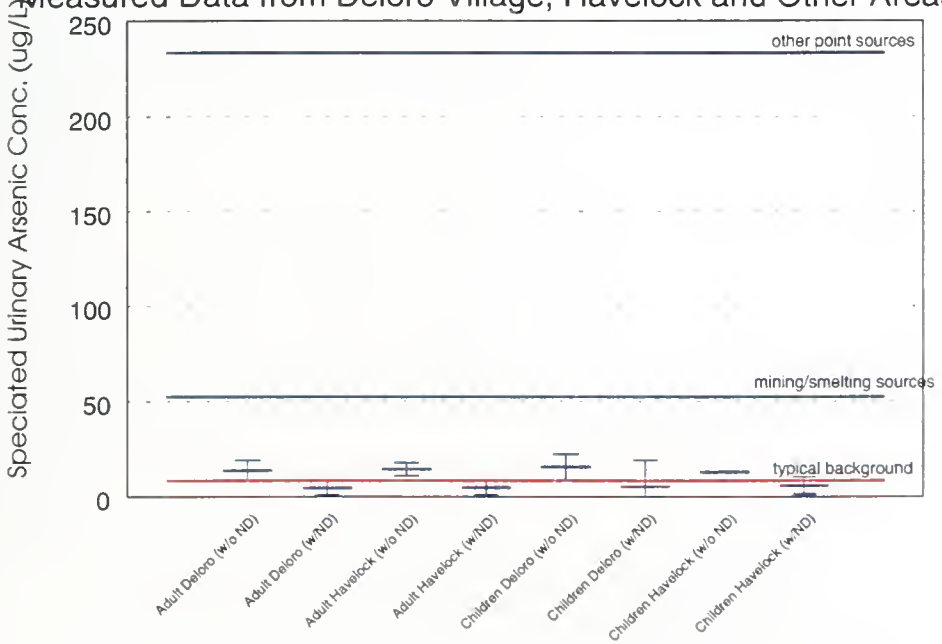
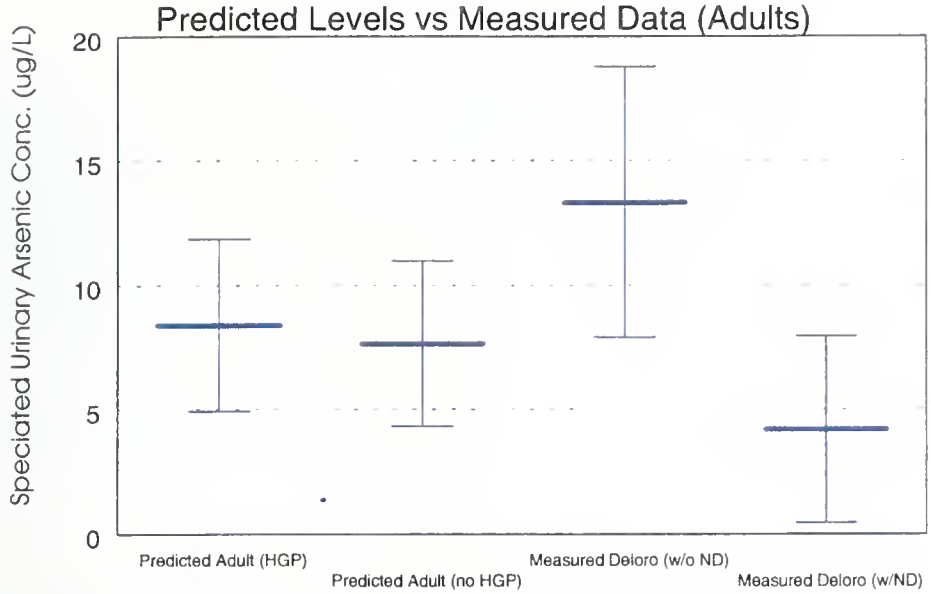
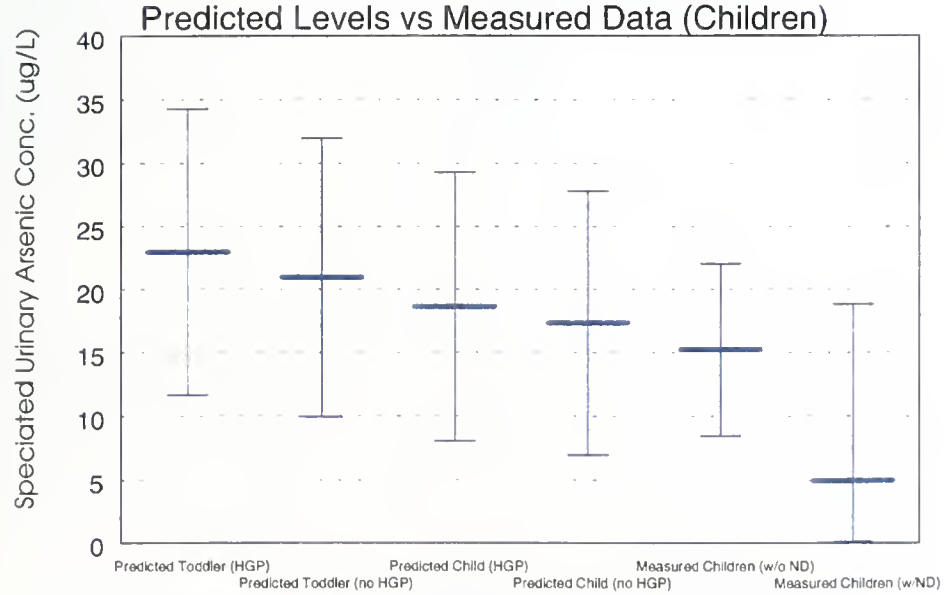


Figure 5-38
Speciated Urinary Arsenic Concentrations
Predicted Levels vs Measured Data (Adults)



Note: The two measured data sets include and exclude non-detectable levels. HGP represents consumption of home grown produce

Figure 5-39
Speciated Urinary Arsenic Concentrations
Predicted Levels vs Measured Data (Children)



Note: The two measured data sets include and exclude non-detectable levels. HGP represents consumption of home grown produce

Figure 40

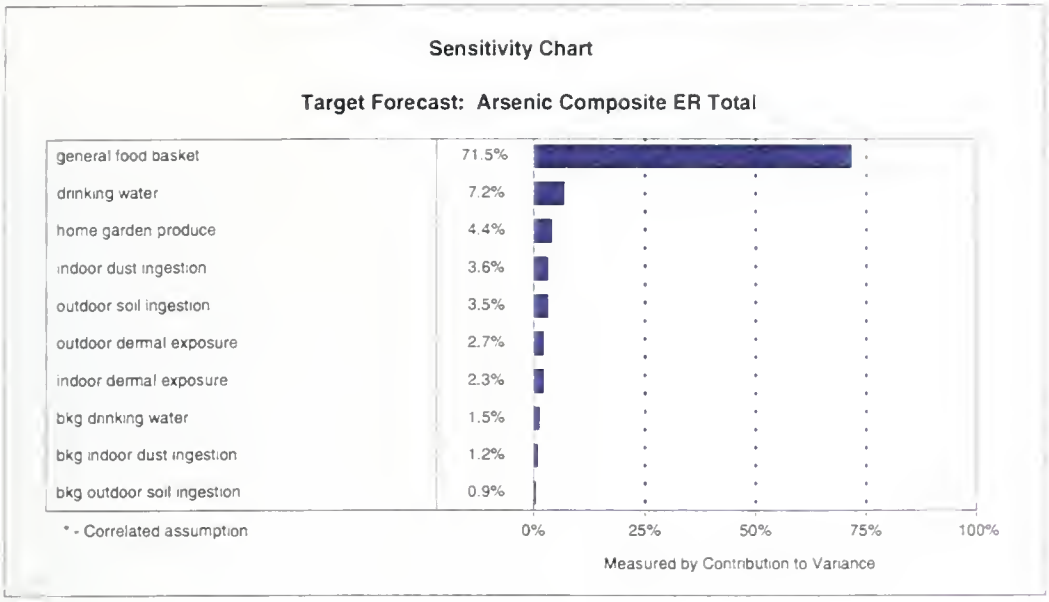


Figure 41

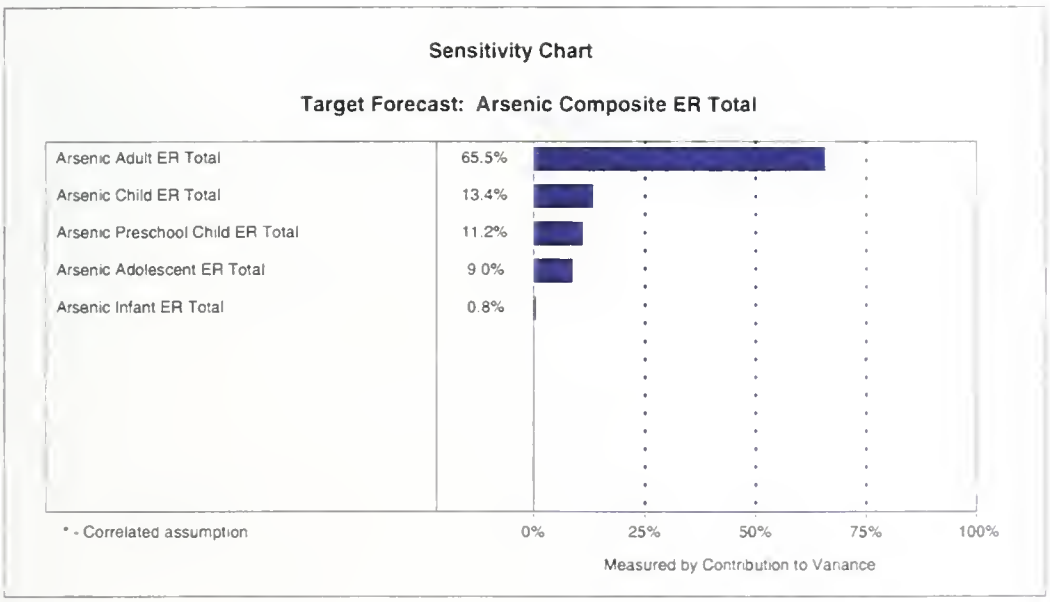


Figure 42

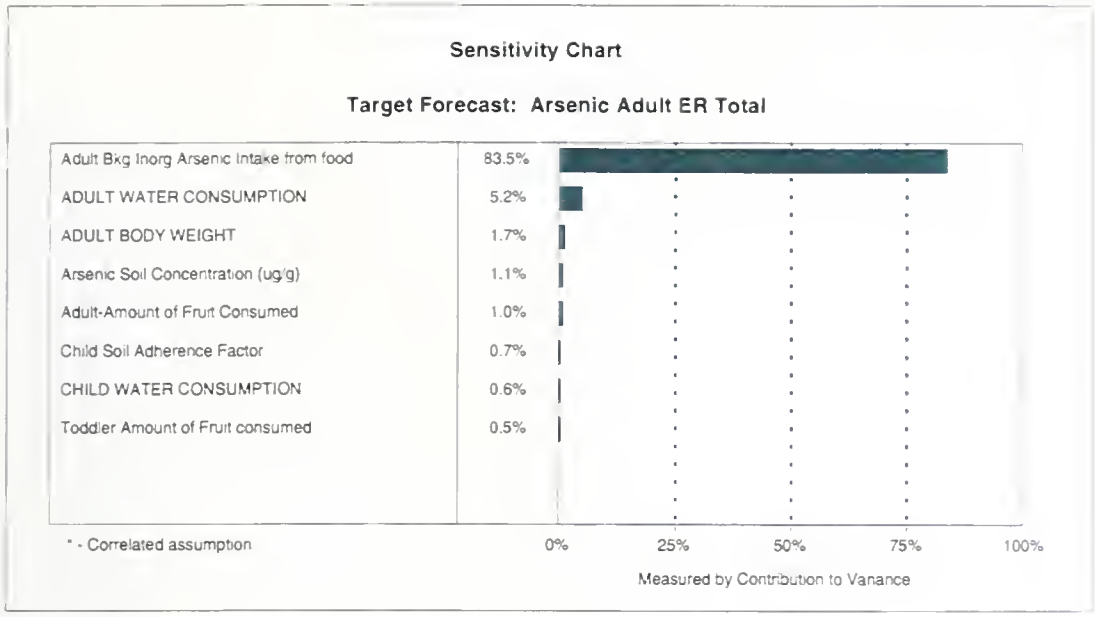
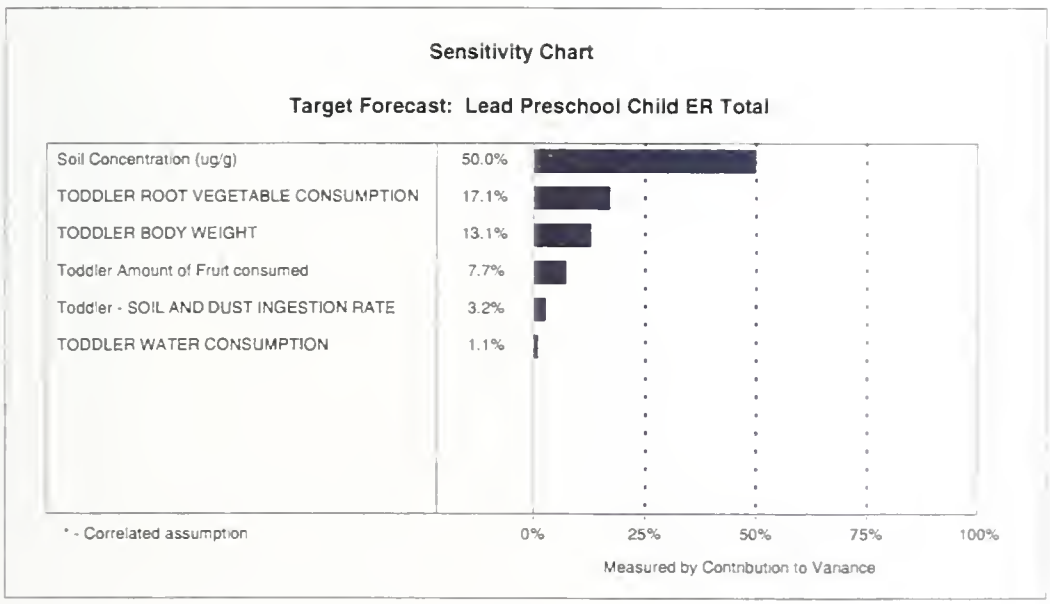


Figure 43



CANTOX ENVIRONMENTAL

DELORO VILLAGE
EXPOSURE ASSESSMENT AND HEALTH RISK CHARACTERIZATION FOR ARSENIC AND OTHER METALS

PART 6 - RISK MANAGEMENT: EXPOSURE AND/OR RISK MITIGATION

December, 1999

PART 6
RISK MANAGEMENT: EXPOSURE AND/OR RISK MITIGATION

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PART 6
RISK MANAGEMENT: EXPOSURE AND/OR RISK MITIGATION

1.0 ARSENIC

The results of the probabilistic risk characterization indicated that for arsenic, the predicted risks of skin cancer to Deloro residents were marginally greater than that for typical Ontario residents. The results of the urinary arsenic evaluation can be used as a form of "reality check" for the exposure assessment and the risk characterization. Based on the exposure assessment, the urinary arsenic model predicted urinary concentration slightly greater than the observed concentrations of Deloro and typical Ontario residents. This can be interpreted as indicating that the exposure assessment was conservative, and likely overestimated risks. In addition, the concentrations of arsenic in urine of Deloro residents were comparable to that of Havelock residents and typical Ontario residents, as indicated by the published literature. Therefore, the marginal increase in ER values observed for Deloro residents in comparison to typical Ontario residents are not considered to be indicative of measurable health risks of Deloro residents.

The current risk assessment indicated that exposures associated with direct soil and dust pathways did not contribute significantly to overall risks of Deloro residents. Thus remediation of the mine site would not be expected to measurably impact the estimated risks; however, such remediation would prevent future contamination of Deloro by arsenic, and would thus ensure that conditions in Deloro improved in future. If deemed necessary, the following options would mitigate future contamination of environmental media in Deloro by preventing mobilization from the site:

- stabilization of tailings;
- capping, or covering the contaminated soil or tailings with clean topsoil;
- excavation of heavily contaminated soils;
- solidification/stabilization limits contaminant mobility, although this is considered to need further research before it could be considered a candidate technology for the mitigation of arsenic exposure.

The results of the urinary arsenic evaluation were sufficient to allow the conclusion that this "snap-shot" of exposures experienced by Deloro residents in September are within the range of concentrations reported for Havelock, and within the range of individuals not exposed to any point sources of arsenic.

1.1 Former Mine Site: Trespassing Scenario

For arsenic, the risk characterization indicated that trespassing on the former mine site was a potentially significant contributor to risk for Deloro residents. Given this, and given the inherent uncertainties in the estimation of the exposures and risks *via* this scenario (regarding time activity patterns, types of exposure, and distribution of concentrations on the mine site), some mitigation of mine site exposures should be considered. This may involve restriction

access to the areas of the site with extremely high concentrations, or in some way preventing exposure to these extreme concentrations (*e.g.*, capping, stabilization, excavation).

2.0 LEAD

The risk characterization for lead indicated that in the absence of the consumption of home garden produce, the risks predicted for Deloro residents were mainly due to exposures to lead in background sources (general food basket, drinking water). Exposures associated with environmental media within Deloro were negligible in the absence of home garden produce.

Although the maximum probabilistic ER values for lead indicated exposures exceeding the criterion based on neurological effects, with the consumption of home garden produce, an exceedence of this magnitude was not considered to be of concern, given the conservatism inherent in this risk assessment. Conservatisms include the basis for the toxicological criterion (the lowest effective blood lead level reported for the most sensitive receptors), the use of the entire range of concentrations throughout Deloro in the estimation of exposure included concentrations, not just those in back yards and gardens. The soil concentrations in Deloro are comparable to the range for Ontario urban soils, and are at or below soil concentration thresholds for elevated blood lead levels in children, as predicted by the IU/BK and SEGH models (OMOE), and by several epidemiological studies. Therefore it was concluded that no remediation was required for lead.

3.0 COBALT, NICKEL, AND SILVER

Based on the comparison to both background risks and the benchmark of safety, it was concluded that the exposures to cobalt, nickel, and silver associated with environmental media in Deloro would not be associated with measurable risks of adverse health effects. As a result, no exposure or risk mitigation would be required for these metals.

CANTOX ENVIRONMENTAL

DELORO VILLAGE
EXPOSURE ASSESSMENT AND HEALTH RISK CHARACTERIZATION FOR ARSENIC AND OTHER METALS

PART 7 - DISCLAIMER

December, 1999

PART 7
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CANTOX ENVIRONMENTAL

DELORO VILLAGE
EXPOSURE ASSESSMENT AND HEALTH RISK CHARACTERIZATION FOR ARSENIC AND OTHER METALS

APPENDIX A - MODELLING PARAMETERS: RECEPTOR PARAMETERS AND ESTIMATION OF INHALATION BIOAVAILABILITY

December, 1999

APPENDIX A
MODELLING PARAMETERS: RECEPTOR PARAMETERS AND ESTIMATION OF INHALATION BIOAVAILABILITY

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APPENDIX A MODELLING PARAMETERS: RECEPTOR PARAMETERS AND ESTIMATION OF INHALATION BIOAVAILABILITY

A-1.0 RECEPTOR PARAMETERS

As recommended by Scott Fleming (OMOE), the Compendium of Canadian Human Exposure Factors for Risk Assessment (Richardson, 1997) has been used as a primary source of probabilistic human receptor data. In cases where this data set was unable to adequately describe certain time-activity patterns and/or behaviourial/physiological characteristics, other data sources, such as the U.S. EPA Activity Factors Hand Book (U.S. EPA, 1997) were used. The following tables are a list of suggested probabilistic parameters which could be used in the current exposure assessment of Deloro residence. For the deterministic assessment, the mean (typical) and plausible maximum (mean ± 2 standard deviations) were used in two separate exposure scenarios.

Table A-1 Nursing Infant Receptor (0 < 6 months)

Receptor Parameter	Plausible Maximum	Mean (typical)	S.D.	Minimum	Maximum	Distribution Type	Reference
Body Weight (kg)	8.2	8.2	2.9			lognormal	O'CONNOR, 1997
Area of Exposed Skin during Winter days (m^2)	0.107	0.0851				linked to whole body surface	O'CONNOR, 1997; Anderson *et al.*, 1985
Area of Exposed Skin during Summer day (m^2)	0.264	0.209				linked to whole body surface	O'CONNOR, 1997; Anderson *et al.*, 1985
Whole Body Surface Area (m^2)	0.457	0.362	0.054			lognormal	O'CONNOR, 1997
Soil Adherence Factor ($g/m^2/d$)	10	5.85		1.7	10	uniform	U.S. EPA, 1992
Amount of Soil/Dust Ingested (g/d)[1]	0.20	0.08	0.126	0.00218	0.20	lognormal	OMOE, 1998; Thompson and Burmaster, 1991
Amount of Air Inhaled (m^3/d)	3.20	2.1	0.6			lognormal	O'CONNOR, 1997
Fraction of Fruit from Home Garden	0%	0%					Calculated; (Refer to Part 5)
Fraction of Fruit Vegetables from Home Garden	0%	0%					Calculated (Refer to Part 5)
Amount of Water Consumed (L/d)	0.677	0.3	0.2			lognormal	O'CONNOR, 1997
Amount of Root Vegetables Consumed (g/d)	191.96	83	58			lognormal	O'CONNOR, 1997
Amount of Fruit and Juices Consumed (g/d)	316.21	136	96			lognormal	O'CONNOR, 1997

Table A-1 Nursing Infant Receptor (0 < 6 months)

Receptor Parameter	Plausible Maximum	Mean (typical)	S.D.	Minimum	Maximum	Distribution Type	Reference
Amount of Other Vegetables Consumed (g/d)	233.5	72	59			lognormal	O'CONNOR, 1997
Amount of time spent outdoors in Deloro during the summer (hrs./wk)	18.38	18.38					Town Survey
Amount of time spent indoors in Deloro during the summer (hrs./wk)	128.63	128.63					Town Survey
Amount of time spent outdoors in Deloro during the winter (hrs./wk)	12.25	12.25					Town Survey
Amount of time spent indoors in Deloro during the winter (hrs/wk)	134.75	134.75					Town Survey

Notes: Root vegetables include carrots, onions, rutabagas, turnip, beets, potatoes (raw, boiled, canned, french fries, chips).
Other vegetables include corn, cabbage (including coleslaw), celery, green peppers, lettuce, cauliflower, broccoli, green beans, peas, tomatoes (fresh or canned, tomato-based condiments), mushrooms, cucumbers (fresh or cucumber-based condiments), baby food vegetables, asparagus, rhubarb, greens, squash, popcorn, beans (white, beans with pork, etc).

[1] The probability distribution reported by Thompson and Burmaster, 1991 has been truncated at the plausible maximum soil ingestion rate of 0.200 mg/day (EPA, 1998) for non-pica children

Table A-2 Preschool Child Receptor (7 months - 4 years)

Receptor Parameter	Plausible Maximum	Mean (typical)	S.D.	Minimum	Maximum	Distribution Type	Reference
Body Weight (kg)	16.5	16.5	4.5			lognormal	O'CONNOR, 1997
Area of Exposed Skin during Winter days (m^2)	0.200	0.153				linked to whole body surface	O'CONNOR, 1997; Anderson *et al.*, 1985
Area of Exposed Skin during Summer day (m^2)	0.463	0.356				linked to whole body surface	O'CONNOR, 1997; Anderson *et al.*, 1985
Whole Body Surface Area (m^2)	0.799	0.613	0.105			lognormal	O'CONNOR, 1997
Soil Adherence Factor ($g/m^2/d$)	10	5.85		1.7	10	uniform	U.S. EPA, 1992
Amount of Soil/Dust Ingested (g/d)[1]	0.200	0.80	0.126	0.00218	0.20	lognormal	Thompson and Burmaster, 1991; EPA 1998
Amount of Air Inhaled (m^3/d)	14.06	9.3	2.6			lognormal	O'CONNOR, 1997

Table A-2 Preschool Child Receptor (7 months - 4 years)

Receptor Parameter	Plausible Maximum	Mean (typical)	S.D.	Minimum	Maximum	Distribution Type	Reference
Fraction of Fruit from Home Garden	2.7%	2.7%					Calculated; (Refer to Part 5)
Fraction of Fruit Vegetables from Home Garden	7.4%	7.4%					Calculated (Refer to Part 5)
Amount of Water Consumed (L/d)	1.35	0.6	0.4			lognormal	O'CONNOR, 1997
Amount of Root Vegetables Consumed (g/d)	271.79	105	91			lognormal	O'CONNOR, 1997
Amount of Fruit and Juices Consumed (g/d)	579.14	234	186			lognormal	O'CONNOR, 1997
Amount of Other Vegetables Consumed (g/d)	195.36	67	74			lognormal	O'CONNOR, 1997
Amount of time spent outdoors in Deloro during the summer (hrs./wk)	26.33	18.38					Town Survey
Amount of time spent indoors in Deloro during the summer (hrs./wk)	128.63	120.66					Town Survey
Amount of time spent outdoors in Deloro during the winter (hrs./wk)	12.25	12.25					Town Survey
Amount of time spent indoors in Deloro during the winter (hrs/wk)	134.75	134.75					Town Survey

Notes: Root vegetables include carrots, onions, rutabagas, turnip, beets, potatoes (raw, boiled, canned, french fries, chips).
Other vegetables include corn, cabbage (including coleslaw), celery, green peppers, lettuce, cauliflower, broccoli, green beans, peas, tomatoes (fresh or canned, tomato-based condiments), mushrooms, cucumbers (fresh or cucumber-based condiments), baby food vegetables, asparagus, rhubarb, greens, squash, popcorn, beans (white, beans with pork, etc).

[1] The probability distribution reported by Thompson and Burmaster, 1991 has been truncated at the plausible maximum soil ingestion rate of 0.200 mg/day (EPA, 1998) for non-pica children

Table A-3 Child Receptor (5 years - 11 years)

Receptor Parameter	Plausible Maximum	Mean (typical)	S.D.	Minimum	Maximum	Distribution Type	Reference
Body Weight (kg)	32.9	32.9	8.9			lognormal	O'CONNOR, 1997
Area of Exposed Skin on a winter day (m^2)	0.2.73	0.178				linked to whole body surface	O'CONNOR, 1997; Anderson *et al.*, 1985

Table A-3 Child Receptor (5 years - 11 years)

Receptor Parameter	Plausible Maximum	Mean (typical)	S.D.	Minimum	Maximum	Distribution Type	Reference
Area of Exposed Skin on a summer day (m^2)	0.784	0.589				linked to whole body surface	O'CONNOR, 1997; Anderson *et al.*, 1985
Whole Body Surface Area (m^2)	1.35	1.014	0.191			lognormal	O'CONNOR, 1997
Soil Adherence Factor ($g/m^2/d$)	10	5.85		1.7	10	uniform	U.S. EPA, 1992
Amount of Soil/Dust Ingested (g/d)[1]	0.200	0.08	0.126	0.00218	0.2	lognormal	Thompson and Burmaster, 1991; EPA, 1998
Amount of Air Inhaled (m^3/d)	20.27	14.5	3.2			lognormal	O'CONNOR, 1997
Fraction of Fruit from Home Garden	2.7%	2.7%					Calculated; (Refer to Part 5)
Fraction of Fruit Vegetables from Home Garden	7.4%	7.4%					Calculated (Refer to Part 5)
Amount of Water Consumed (L/d)	1.56	0.8	0.4			lognormal	O'CONNOR, 1997
Amount of Root Vegetables Consumed (g/d)	425	161	145			lognormal	O'CONNOR, 1997
Amount of Fruits and Juices Consumed (g/d)	699.41	268	236			lognormal	O'CONNOR, 1997
Amount Other Vegetables Consumed (g/d)	287.88	98	110			lognormal	O'CONNOR, 1997
Amount of time spent outdoors in Deloro during the summer (hrs./wk)	26.33	14.00		14.00	26.33	uniform	Town Survey
Amount of time spent indoors in Deloro during the summer (hrs./wk)	120.66	98.00		98.00	128.63	uniform	Town Survey
Amount of time spent outdoors in Deloro during the winter (hrs./wk)	12.25	9.30		9.30	12.28	uniform	Town Survey
Amount of time spent indoors in Deloro during the winter (hrs/wk)	134.75	103.00		103.00	134.75	Uniform	Town Survey

Notes: Root vegetables include carrots, onions, rutabagas, turnip, beets, potatoes (raw, boiled, canned, french fries, chips).
Other vegetables include corn, cabbage (including coleslaw), celery, green peppers, lettuce, cauliflower, broccoli, green beans, peas, tomatoes (fresh or canned, tomato-based condiments), mushrooms, cucumbers (fresh or cucumber-based condiments), baby food vegetables, asparagus, rhubarb, greens, squash, popcorn, beans (white, beans with pork, etc).

[1] The probability distribution reported by Thompson and Burmaster, 1991 has been truncated at the plausible maximum soil ingestion rate of 0.200 mg/day (EPA, 1998) for non-pica children

Table A-4 Adolescent Receptor (12 years - 19 years)

Receptor Parameter	Plausible Maximum	Mean (typical)	S.D.	Min.	Max.	Distribution Type	Reference
Body Weight (kg)	59.7	59.7	13.5			lognormal	O'CONNOR, 1997
Area of Exposed Skin on a winter day (m^2)	0.270	0.215				linked to whole body surface	O'CONNOR, 1997; Anderson *et al.*, 1985
Area of Exposed Skin on a summer day (m^2)	1.16	0.925				linked to whole body surface	O'CONNOR, 1997; Anderson *et al.*, 1985
Whole Body Surface Area (m^2)	1.94	1.547	0.225	(9-11yrs)		lognormal	O'CONNOR, 1997
Soil Adherence Factor ($g/m^2/d$)	10	5.85		1.7	10	uniform	U.S. EPA, 1992
Amount of Soil/Dust Ingested (g/d)	0.100	0.02		0.02	0.100	uniform	EPA, 1998
Amount of Air Inhaled (m^3/d)	23.08	15.8	4.0			lognormal	O'CONNOR, 1997
Fraction of Fruit from Home Garden	2.7%	2.7%					Calculated; (Refer to Part 5)
Fraction of Fruit Vegetables from Home Garden	7.4%	7.4%					Calculated (Refer to Part 5)
Amount of Water Consumed (L/d)	2.13	1	0.6			lognormal	O'CONNOR, 1997
Amount of Root Vegetables Consumed (g/d)	559.47	227	179			lognormal	O'CONNOR, 1997
Amount of Fruits and Juices Consumed (g/d)	687.92	258	237			lognormal	O'CONNOR, 1997
Amount of Other Vegetables Consumed (g/d)	354.07	120	136			lognormal	O'CONNOR, 1997
Amount of time spent outdoors in Deloro during the summer (hrs./wk)	26.33	12.18		12.18	26.33	uniform	Town Survey
Amount of time spent indoors in Deloro during the summer (hrs./wk)	120.66	85.75		85.75	120.66	uniform	Town Survey
Amount of time spent outdoors in Deloro during the winter (hrs./wk)	12.25	8.17		8.17	12.25	uniform	Town Survey

Table A-4 Adolescent Receptor (12 years - 19 years)

Receptor Parameter	Plausible Maximum	Mean (typical)	S.D.	Min.	Max.	Distribution Type	Reference
Amount of time spent indoors in Deloro during the winter (hrs/wk)	134.75	89.89		89.89	134.75	Uniform	Town Survey

Notes: Root vegetables include carrots, onions, rutabagas, turnip, beets, potatoes (raw, boiled, canned, french fries, chips).
Other vegetables include corn, cabbage (including coleslaw), celery, green peppers, lettuce, cauliflower, broccoli, green beans, peas, tomatoes (fresh or canned, tomato-based condiments), mushrooms, cucumbers (fresh or cucumber-based condiments), baby food vegetables, asparagus, rhubarb, greens, squash, popcorn, beans (white, beans with pork, etc).

Table A-5 Adult Receptor (20 years < 70 years)

Receptor Parameter	Plausible Maximum	Mean (typical)	S.D.	Minimum	Maximum	Distribution Type	Reference
Body Weight (kg)	42.8	70.7	14.5			lognormal	O'CONNOR, 1997
Area of Exposed Skin on a winter day (m^2)	0.260	0.215				linked to whole body surface	O'CONNOR, 1997; Anderson *et al.*, 1985
Area of Exposed Skin on a summer day (m^2)	1.22	1.01				linked to whole body surface	O'CONNOR, 1997; Anderson *et al.*, 1985
Whole Body Surface Area (m^2)	2.13	1.764	0.210			lognormal	O'CONNOR, 1997
Soil Adherence Factor ($g/m^2/d$)	10	5.85		1.7	10	uniform	U.S. EPA, 1992
Amount of Soil/Dust Ingested (g/d)	0.100	0.02		0.02	0.100	uniform	EPA 1998
Amount of Air Inhaled (m^3/d)	22.88	15.8	3.9			lognormal	O'CONNOR, 1997
Fraction of Fruit from Home Garden	2.7%	2.7%					Calculated; (Refer to Part 5)
Fraction of Fruit Vegetables from Home Garden	7.4%	7.4%					Calculated (Refer to Part 5)
Amount of Water Consumed (L/d)	3.014	1.5	0.8			lognormal	O'CONNOR, 1997
Amount of Root Vegetables Consumed (g/d)	467.83	188	151			lognormal	O'CONNOR, 1997
Amount of Fruit and Juices Consumed (g/d)	618.04	245	202			lognormal	O'CONNOR, 1997
Amount of Other Vegetables Consumed (g/d)	369.86	137	129			lognormal	O'CONNOR, 1997
Amount of time spent outdoors in Deloro during the summer (hrs./wk)	18.38	12.18		12.18	18.38	uniform	Town Survey

Table A-5 Adult Receptor (20 years < 70 years)

Receptor Parameter	Plausible Maximum	Mean (typical)	S.D.	Minimum	Maximum	Distribution Type	Reference
Amount of time spent indoors in Deloro during the summer (hrs./wk)	128.63	85.75		85.75	128.63	uniform	Town Survey
Amount of time spent outdoors in Deloro during the winter (hrs./wk)	12.25	8.17		8.17	12.25	uniform	Town Survey
Amount of time spent indoors in Deloro during the winter (hrs/wk)	134.75	89.90		89.90	134.75	Uniform	Town Survey

Notes: Root vegetables include carrots, onions, rutabagas, turnip, beets, potatoes (raw, boiled, canned, french fries, chips).
Other vegetables include corn, cabbage (including coleslaw), celery, green peppers, lettuce, cauliflower, broccoli, green beans, peas, tomatoes (fresh or canned, tomato-based condiments), mushrooms, cucumbers (fresh or cucumber-based condiments), baby food vegetables, asparagus, rhubarb, greens, squash, popcorn, beans (white, beans with pork, etc).

A-2.0 ESTIMATION OF BIOAVAILABILITY VIA INHALATION

A-2.1 Assumptions Regarding Bioavailability *Via* Inhalation

The bioavailability of chemicals when inhaled is dependent on whether the chemical is bound to particulate matter, or exists as a vapour in the atmosphere. Higher molecular weight chemicals are usually adsorbed or bound to airborne particles in the environment (*e.g.*, diesel exhaust particles, various types of fly ash, crude airborne particles, soot from various combustion sources) rather than remaining in the vapour phase (Albagli *et al.*, 1974; Starkey and Warpinski, 1974; Pierce and Katz, 1975; Potts and Oberdorster, 1983). Smaller molecular weight chemicals with high vapour pressures exist primarily in the vapour phase. The bioavailability *via* inhalation of chemicals bound to particulates is discussed in detail in Section 4.2.1; the bioavailability of chemicals *via* inhalation that exist in the vapour phase is discussed in detail in Section 4.2.2.

A-2.1.1 Bioavailability of Chemicals from Inhaled Particles

To enter the body, chemicals bound to particulate matter must be desorbed from the particles either before absorption into tissues or after uptake into cells by phagocytosis (Potts and Oberdorster, 1983). Even some of the chemicals on particles entering cells by phagocytosis (*e.g.*, pulmonary macrophages) would not be considered directly bioavailable to the body because these cells can be shed from the surfaces of the respiratory system into mucous lining the respiratory system, cleared by the mucociliary apparatus and ingested (Brain and Mosier, 1980; Lioy *et al.*, 1985).

In order to develop a common base for the assessment of the bioavailability of chemicals associated with airborne particles, a standardized description of the dynamics of particle distribution in various regions of the respiratory system has been developed and is outlined in the following sections. This information was used to estimate the bioavailability of airborne emissions associated with particles.

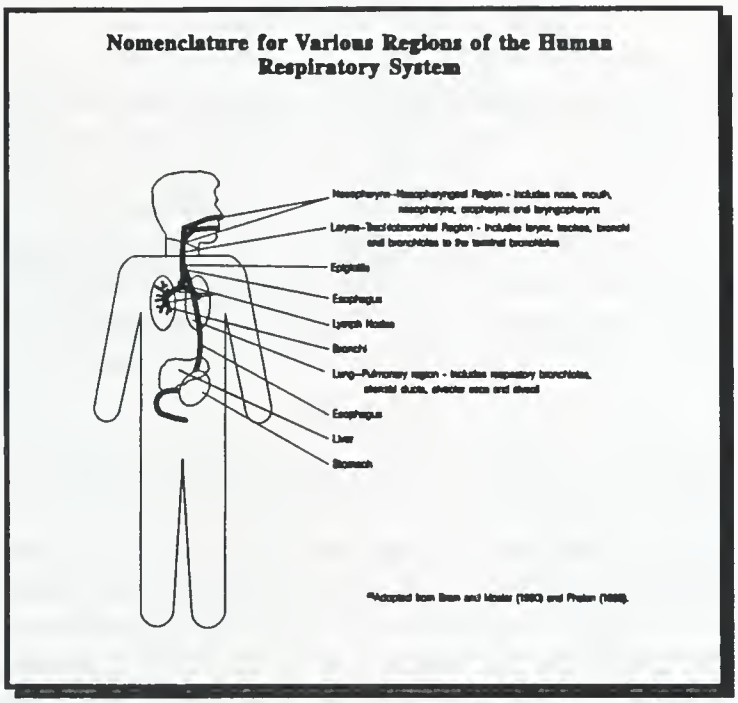
There are a large number of factors that determine the bioavailability of chemicals from airborne particles in the respiratory system. The major factors include the physical properties of the airborne particles (*e.g.*, aerodynamic diameter, geometrical diameter, shape, electric charge, material density), air velocity in the respiratory tract and adsorption characteristics of the chemical to the particles (Potts and Oberdorster, 1983). The significance of these factors on the bioavailability of airborne chemical emissions has been evaluated by estimating:

- the fraction of the airborne particles that would be deposited in various regions of the respiratory system;
- the fraction of the deposited airborne particles that would be retained in the respiratory system;
- the fraction of the deposited particles that would be cleared from the respiratory system and swallowed, thereby entering the gastrointestinal tract;
- the fraction of the chemical on airborne particles retained by the respiratory systems that would be absorbed; and,
- the fraction of the chemical that would be absorbed from the gastrointestinal tract following clearance from the respiratory system.

The first 3 of these factors are discussed in the following sections. The last 2 factors, mentioned above, are chemical specific and would be applied in the estimation of the bioavailability of individual chemicals.

The dynamics of airborne particles varies substantially in different regions of the respiratory system. To assist in clarifying the following discussions of the deposition, retention and clearance of airborne particles from the respiratory system, the terminology used to describe the various regions of the respiratory system have been outlined in Figure A-1. For the purpose of this assessment, it was assumed that particles inhaled by the various terrestrial animal receptors will act in a similar manner as those inhaled by human receptors.

Figure A-1 Regions of the Respiratory System



A-2.1.1.1 Fraction of Total Airborne Particles Deposited in the Respiratory System

Particle size directly affects the fraction of airborne particles that are deposited in various regions of the respiratory system (Brain and Mosier, 1980; Lioy *et al.*, 1985) and therefore, the potential delivery of chemicals bound to these particles to body tissues. Deposition is a measure of the fraction of inspired particles caught by the respiratory tract and not exhaled (Brain and Mosier, 1980; Lioy *et al.*, 1985). Generally, only particles less than 10 micrometres (um) in mass median aerodynamic diameter (MMAD) gain access to and may be deposited in the lower regions of the respiratory system, and only particles less than about 2.5 um MMAD actually reach the pulmonary region (Potts and Oberdorster, 1983; Lioy *et al.*, 1985; Klaassen *et al.*, 1986; Paustenbach, 1987).

For particle sizes ranging from 0.1 um to 1 um MMAD, the primary factors affecting deposition in the respiratory system are sedimentation and diffusion from the air stream onto the respiratory surfaces. Inertial impaction and interception are the primary factors affecting the deposition of particles <10 um MMAD (Brain and Mosier, 1980; NRC, 1986). Substantial fractions of airborne particles in the respirable size range, especially less than 1 um, are exhaled from the respiratory system without deposition (Brain and Mosier, 1980; Potts and Oberdorster, 1983; Lioy *et al.*, 1985). Therefore, information on the particle size distribution in ambient air is needed to estimate the total fraction of airborne particles deposited in the respiratory system.

According to U.S. EPA data (U.S. EPA, 1977), the typical distribution of particle sizes in

dusts generated from dirt roads is 8% <5 um, 24% between 5 and 30 um, and 68% between 30 and 100 um. Dusts generated from gravel roads have greater amounts of finer particles; normally with about 23% <5 um, 39% between 5 and 30 um, and 38% between 30 and 100 um. Dusts generated from soils are important in estimating chemical exposures from multiple sources because the chemicals are deposited onto soils from ambient sources. However, chemicals bound to airborne particles other than those derived from soil have a different size distribution.

According to more recent information from the U.S. EPA (1984), atmospheres with a total suspended particle concentration of 75 mg/m^3 contain approximately 50 mg/m^3 of particles <10 um. Based on these data about 66% (50/75) of the total particles in air, exclusive of specific dusts derived from dirt or gravel roads as discussed earlier, are in the respirable range.

The fractions of 3 different sizes of particles that would be deposited in various regions of the respiratory system are summarized in Table A-6. These estimates were calculated using a computer model of lung dynamics of the deposition of particles of different MMAD (Task Group on Lung Dynamics, 1966; Brain and Mosier, 1980). The estimated fractions of particles deposited in the nasopharyngeal, tracheobronchial and pulmonary regions of the respiratory system were 0.8 to 2.4%, 2.9 to 3.6%, and 41.2 to 42.3%, respectively for 0.2 um MMAD particles, 50.2 to 50.7%, 3.6 to 4.3%, and 21 to 23.6%, respectively for 2.0 um MMAD particles, and 95.6 to 97.2%, 0.8 to 1%, and 1.7 to 2.6%, respectively for 20 um MMAD particles (see Table A-6 derived from Brain and Mosier, 1980). The results reported from the lung dynamics model indicate that substantial fractions of larger particles (*e.g.*, 96 to 98% of 20 um and 54 to 55% of the 2 um particles) are deposited in the nasopharyngeal/tracheobronchial regions, whereas most of the 0.2 um MMAD particles which become deposited in the respiratory system are deposited in the pulmonary region (*e.g.*, 41 to 42%). Substantial fractions of smaller particles would be exhaled without deposition (*e.g.*, the difference between the total airborne fraction and amount deposited, namely 21 to 25% for 2.0 um particles and 52 to 55% for 0.2 um particles).

Table A-6 Fraction (%)[a] of Total Airborne Particles Deposited in the Respiratory System[b]

Size (um MMAD)	Region Of The Respiratory System				Total Deposited[c]
	NP	TB	NP+TB	P	
0.2	0.8-2.4	2.9-3.6	3.7-6.0	41.2-42.3	44.9-48.3
2	50.2-50.7	3.6-4.3	53.8-55.0	21.0-23.6	74.8-78.6
20	95.6-97.2	0.8-1.0	96.4-98.2	1.7-2.6	98.1-100.8

[a] Note that the percentage particles deposited in the respiratory system do not add to 100% because a fraction of the airborne particles are exhaled and not deposited.
[b] Adapted from Brain and Mosier (1980).
[c] Sum of (NP+TB) + P, representing the total fraction of the airborne particles deposited in all regions of the respiratory system.
NP Nasopharyngeal region of the respiratory system, also known as a part of the upper respiratory tract.
TB Tracheobronchial region of the respiratory system, also known as a part of the upper respiratory tract.
P Pulmonary region of the respiratory system, also known as a part of the lower respiratory tract.

A number of studies are also available that provide direct measurements of the fractions of different sized particles deposited in the respiratory system. Studies on the retention by rats of gallium oxide particles averaging 0.1 um MMAD demonstrated that 19.2% of the total dose of particles inhaled was deposited in the respiratory system (tracheobronchial and pulmonary regions) (Sun *et al.*, 1982). In general agreement with these data, other studies using gallium oxide particles reported deposition fractions of 15% (Wolff *et al.*, 1982) and 25% (Wolff *et al.*, 1981) for rats and dogs, respectively. A deposition of 15% also was reported for 0.1 to 0.15 um MMAD diesel particles in rats (Chan *et al.*, 1981). Studies using 0.6 um MMAD polystyrene-latex spheres in humans demonstrated about 10% deposition. Similar results were reported using 0.5 um and 0.2 to 1.0 um MMAD aerosols (NRC, 1986). These measured values show a much narrower range than those derived from the computer model discussed above; however, the size range of particles used in the experimental studies was not nearly as wide as those assessed using the computer model.

Since a wide range of particle sizes would be expected in ambient air, the data derived from the computer model was considered more relevant to general environmental particles and has been used in the estimation of the bioavailability of chemicals from airborne particles as required for the calculation of inhalation absorption values.

A-2.1.1.2 Fraction of Total Airborne Particles Retained by the Respiratory System and the Fraction Cleared and Ingested

The data presented in the previous section demonstrate that the fraction of particles deposited can range from <1 to 97%, depending on the size of the particles and in the respiratory system. However, only a fraction of the particles deposited remain in the respiratory system for an appreciable length of time (*i.e.*, designated "retained particles" because of slow clearance half-lives in the range of 65 to 90 days) (Brain and Mosier, 1980; Sun *et al.*, 1982). The remainder of the particles are rapidly cleared from the respiratory system either in the expired air or by the mucociliary apparatus (*i.e.*, designated "cleared particles" because of

clearance half-lives of minutes to a few hours) (Brain and Mosier, 1980).

The mechanisms of clearance of particles from the respiratory system, primarily *via* the mucociliary apparatus, are extremely efficient (Brain and Mosier, 1980; Lioy *et al.*, 1985). Data from coal miners with black lung disease indicated that less than 10% of the dust originally deposited in the respiratory system was retained (Brain and Mosier, 1980). Particles deposited on the upper respiratory system can be rapidly removed by the mucociliary apparatus. Particles also can be removed from the pulmonary region although the mechanisms are less clear for this region (Brain and Mosier, 1980; Lioy *et al.*, 1985). In humans, the rate of mucous transport in the trachea has been estimated at 1 to 2 cm/minute (Lioy *et al.*, 1985; NRC, 1986). This means that a substantial portion of the particles would be rapidly transported (*e.g.*, within minutes to a few hours) into the larynx by the action of the mucociliary apparatus (Brain and Mosier, 1980; Lioy *et al.*, 1985). In assessing the bioavailability of chemicals associated with airborne particles, it is important to recognize that particles cleared by the mucociliary apparatus are then either swallowed or removed in sputum (Brain and Mosier, 1980; Wolff *et al.*, 1982; Potts and Oberdorster, 1983; Morgan *et al.*, 1984; Lioy *et al.*, 1985). The removal of particles in sputum is more significant under conditions of high ambient dust levels; however, some losses occur through such mechanisms under normal ambient dust conditions. In addition, some of the airborne particles would be trapped by the nares and nasal hairs and would be normally removed by blowing mucous from the nose. For the estimation of the bioavailability of chemicals bound to particulates, the fraction of airborne particles removed in sputum or lost in mucous from the nose have not been estimated, rather it has been conservatively assumed that 100% of the particles that are rapidly cleared from the respiratory system by the mucociliary apparatus are subsequently ingested. A fraction of the chemicals adsorbed to such particles would then be bioavailable through the gastrointestinal tract.

The fractions of different sized particles cleared from the respiratory system have been estimated indirectly by Brain and Mosier (1980) using the Task Group on Lung Dynamics (1966) mathematical model describing the dynamics of particle deposition/retention by the respiratory system. The estimates derived for Class W particles [moderate retention and intermediate clearance rates (weeks) from the pulmonary region] or Class Y particles [avid retention and slow clearance rates (years) from the pulmonary region] indicate that 90 and 99%, respectively, of the particles deposited in the nasopharyngeal/tracheobronchial regions would be rapidly cleared. It has been conservatively assumed that the particles to which chemicals are adsorbed would be in either of these 2 classes rather than Class D (minimal retention and rapid clearance from the pulmonary region) (Brain and Mosier, 1980).

In the estimation of the bioavailability of airborne chemicals on particulates, it has been assumed, based on the above information, that all the particles (*e.g.*, 100%) that were deposited in the nasopharyngeal/tracheobronchial regions are rapidly cleared and ingested. This would be estimated by the sum of the fraction of different sized particles rapidly cleared in these regions, namely 4 to 6%, 54 to 55% and 96 to 98% for particles of 0.2, 2.0 and 20.0 um MMAD, respectively (see Table A-7).

In addition, an estimated 40% of the Class W and Y particles deposited in the pulmonary region of the respiratory system would be rapidly cleared with a half-life of about 24 hours, and another 40% would be slowly cleared with a half-life of about 90 days (Brain and Mosier, 1980). Therefore, the fraction of the airborne particles cleared rapidly (half-life 24 hours) from the pulmonary region and ingested would be about 16 to 17%, 8 to 9% and 0.7 to 1.0% of the total exposure for 0.2, 2 and 20 um MMAD particles, respectively (see Table A-7). The lung dynamics model indicates that a comparable fraction (*i.e.*, 40%) of such particles would be slowly cleared with a half-life of about 90 days. According to the lung dynamics model, about 20% of the particles deposited would be absorbed from the pulmonary region into the blood and lymphatic systems.

Table A-7 Fraction (%) of Total Airborne Particles Cleared From the Respiratory System[a]

Particle Size (um MMAD)	Fraction Of Total Cleared (%) Region Of The Respiratory System			
	NP+TB	P	NP+TB+P	P
	Cleared Rapidly[b]			Cleared Slowly Or Absorbed[c]
0.2	3.7-6.0	16.5-16.9	20.2-22.9	24.7-25.4
2	53.8-55.0	8.4-9.4	62.2-64.4	12.6-14.2
20	96.4-98.2	0.7-1.0	97.1-99.2	1.0-1.6

[a] Adapted from Brain and Mosier (1980).

[b] Rapid clearance indicates particles cleared from the respiratory system with a half-life of minutes to hours. Values were calculated based on 100% rapid clearance of deposited particles from the NP/TB and 40% rapid clearance from P.

[c] Slow clearance indicated particles cleared from the respiratory system with a half-life of weeks to years. Absorption refers to particles absorbed from the pulmonary region into the blood or lymph. Values were calculated based on 40% slow clearance of deposited particles plus 20% absorption of particles from the pulmonary region into blood or lymph (Brain and Mosier, 1980).

NP Nasopharyngeal region of the upper respiratory system.

TB Tracheobronchial region of the upper respiratory system.

P Pulmonary region of the lower respiratory system.

Experimental data also are available on the fractions of particles rapidly cleared from the respiratory system (*i.e.*, those assumed to be swallowed). Sun *et al.* (1982) demonstrated that of the 19.2% of the 0.1 um gallium oxide particles deposited in the respiratory system of rats, 12 + 3% of the particles were slowly cleared from the lung with a clearance half-life of about 65 days. The remainder of the particles (*i.e.*, 19.2% - 12% = 7.2%) were rapidly cleared from the respiratory system by the mucociliary apparatus and subsequently ingested. For comparable sized particles, these experimental observations agree well with the estimates from computer modelling discussed earlier.

A-2.1.1.3 Summary of Fractions of Total Airborne Particles Retained and Cleared from the Respiratory System

The dynamics of particle deposition, retention and clearance from the lung are critical to the estimation of the bioavailability of chemicals that are associated with airborne particles. The information on particle dynamics in the lung, as presented in the previous sections, has been summarized in Table A-8 and Figure A-2.

Use of the information on airborne particle dynamics in the lung to estimate the bioavailability of chemicals on particulates requires knowledge of the particle sizes. Normal ambient particle size distribution measurements can provide a reasonable estimate of the particle to which populations may be exposed. The distribution of particle sizes in ambient air is about 33% >10 um MMAD and 66% <10 um MMAD (U.S. EPA, 1987). Since lung particle dynamics were modelled for 20, 2 and 0.2 um particles, in order to estimate the total fraction of particles retained in the respiratory system and those swallowed into the gastrointestinal tract, it has been assumed that the total airborne particles are equally distributed among the 3 particle sizes (*i.e.*, 33% of the airborne particles were 20 um MMAD, 33% were 2.0 um and 33% were 0.2 um).

The percentages of the total airborne particles deposited in the entire respiratory system were approximately 45 to 48% for 0.2 um particles, 75 to 79% for 2 um particles and 98 to 100% for 20 um particles (derived from Table A-6). A fraction of these particles of each size would be retained (*i.e.*, very slowly cleared) by the respiratory system. Another fraction would be rapidly cleared and swallowed.

The percentages of the total airborne particles deposited in the respiratory system that would be retained (includes those slowly cleared and absorbed) were approximately 24.7 to 25.4% for 0.2 um particles, 12.6 to 14.2% for 2 um particles and 1.0 to 1.6% for 20 um particles. The total percentage of all airborne particles retained in the respiratory system has been estimated as 12.6 to 13.6% (average 13%). This value was calculated by summation of 33% of the retention values for each of the 3 particle sizes. For the purpose of the assessment of potential exposures to airborne particulates, it has been assumed that 100% of the chemicals on these particles were bioavailable (*i.e.*, a total of 13% of the chemical contained on airborne particles would be absorbed through the respiratory system).

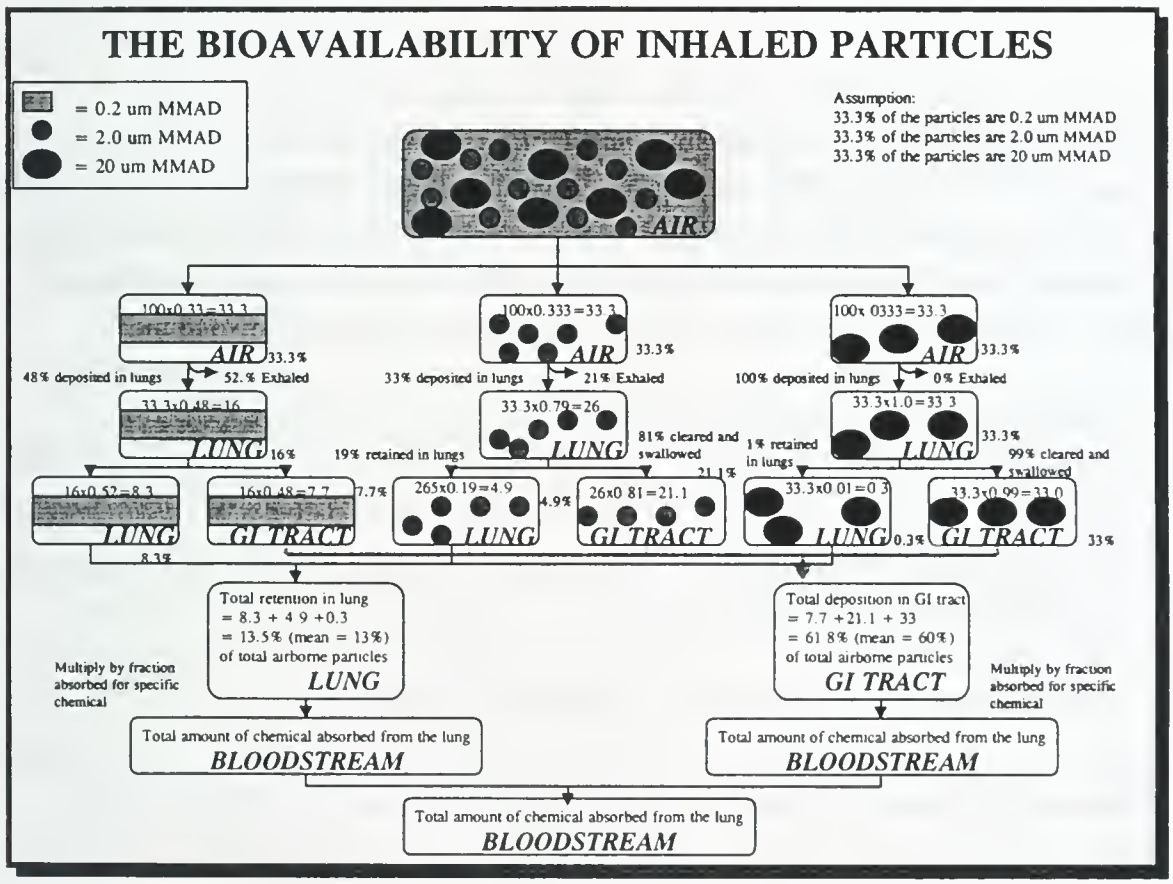
Table A-8 Summary of the Estimated Fraction (%) of Total Airborne Particles Retained[a] and Cleared[a] From the Respiratory System

Size (um MMAD)	Retained (%)	Cleared (%)
0.2	24.7-25.4	20.2-22.9
2	12.6-14.2	62.2-64.4
20	1.0-1.6	97.1-99.2
Total[a]	12.6-13.6	59-61
(Average)[b]	13	60

[a] Based on particles that are slowly cleared plus those absorbed into the blood or lymph, according to Brain and Mosier, 1980 (see Table A-7).

[b] Calculated by summation of 33% of the value for each particle size based on the assumption that the particles sizes are equally distributed in the ambient air.

Figure A-2 Lung Particle Dynamics



The fraction of total airborne particles cleared rapidly from the respiratory tract and swallowed were approximately 20 to 23% for 0.2 um particles, 62 to 64% for 2 um particles and 97 to 99% for 20 um particles (derived from Table A-7). The total percentage of all airborne particles rapidly cleared from the respiratory system has been estimated as 59 to 61% (average 60%). This value was calculated by summation of 33% of the rapid clearance

values for each of the 3 particle sizes. Therefore, 60% of the chemicals on these particles would be swallowed and enter the gastrointestinal tract. The actual dose received from this route would be dependent on the fraction of ingested material absorbed as discussed in the specific assessment of each chemical.

A-2.1.2 Bioavailability of Chemicals in the Gas/Vapour State

In order to develop a common base for the bioavailability assessment of gases/vapours, a standardized description of the behaviour of such chemicals in the respiratory system has been developed and is outlined below. This information was used to estimate the inhalation bioavailability of chemicals in the gas/vapour state.

There are several factors that determine the bioavailability of chemicals existing as gases/vapours in the respiratory system. The major factors include physical properties (*e.g.*, exchange rates of chemical molecules and lung surface), the physical/chemical properties of the chemical (*e.g.*, electric charge, vapour pressure, molecular size), and the air velocity in the respiratory tract. The significance of these factors on the bioavailability of chemicals existing primarily in the vapour phase has been evaluated by estimating:

- the fraction of the chemical that would be deposited in various regions of the respiratory system;
- the fraction of the chemical that would be retained by the respiratory system and absorbed into the body; and,
- the fraction of the chemicals that would not be retained and exhaled.

Chemicals with a diameter of less than 0.2 microns were assumed to exist primarily in a gas/vapour state (C. Baines, Personal Communication). As a result, the fraction of chemicals that would be deposited in various regions of the respiratory system would be approximately 44.9 to 48.3% (see Table A-6). It was assumed the remaining amount of chemical (approximately 50%) would be exhaled and no longer be available for absorption by the respiratory system. Studies on chemicals which exist in the gas/vapour phase, have shown total inhalation bioavailabilities ranging from 15 to 75%.

It should be noted that the length of exposure has a direct effect on the retention of chemicals

in the lungs. For example, it was observed for ammonia that inhalation exposures of only a minute duration resulted in a high retention value (*i.e.*, 75%); however, if the exposure period were lengthened to only 10 minutes, this retention value fell to only 23% (Silverman *et al.*, 1949). This was explained by an attainment of equilibrium for chemical concentrations between the lung and surrounding environment. Equilibrium between inhaled and exhaled carbon disulphide was reported to be attained within 1 to 2 hours of initiation of exposure (McKee *et al.*, 1943; Teisinger and Soucek, 1952; Tazuka, 1955; WHO, 1979). Once equilibrium was attained, the fraction of carbon disulphide retained in the lung ranged from 15 to 45% of the concentration in air (Soucek and Pavelkova, 1953; Warnecke and Bobsien, 1954; Demus, 1967). Thus, exposure to a constant concentration of gas/vapour will result in a decrease in the retention of the gas/vapour in the lung would be expected to decrease with time as a result of the establishment of equilibrium.

Based on the data provided in Table A-6 (for particles <2 um) and about 50 to 80% of chemicals in the gas/vapour phase would be retained by the respiratory system. A bioavailability of 100% has been assumed for gases/vapours retained in the lung (*i.e.*, gases/vapours would not be cleared by the mucociliary apparatus and swallowed).

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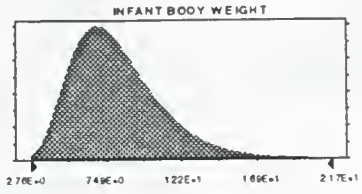
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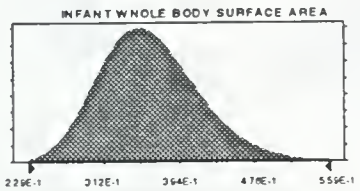
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Assumptions-Probabilistic Receptor Parameters

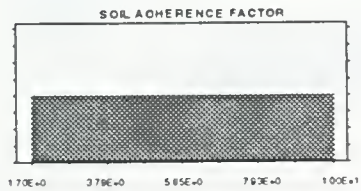
Assumption: INFANT BODY WEIGHT — Cell: E9



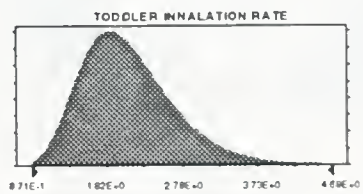
Assumption: INFANT WHOLE BODY SURFACE AREA — Cell: E12



Assumption: SOIL ADHERENCE FACTOR — Cell: E13

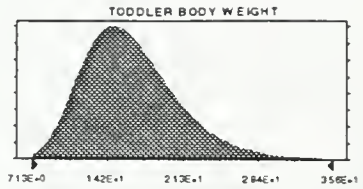


Assumption: TODDLER INHALATION RATE — Cell: E17



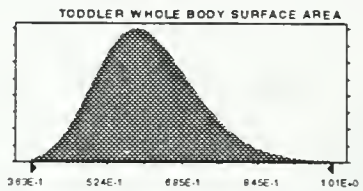
Assumption: TODDLER BODY WEIGHT

Cell: H9



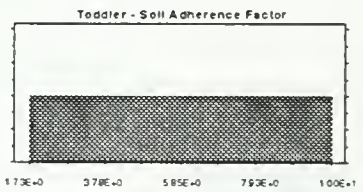
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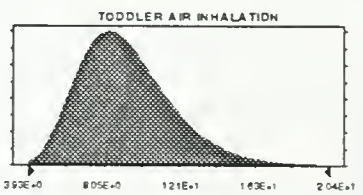
Assumption: Toddler - Soil Adherence Factor

Cell: H13

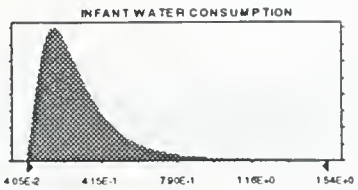


Assumption: TODDLER AIR INHALATION

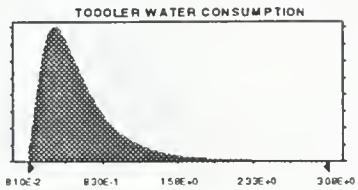
Cell: H17



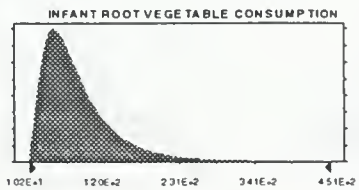
Assumption: INFANT WATER CONSUMPTION **Cell: E29**



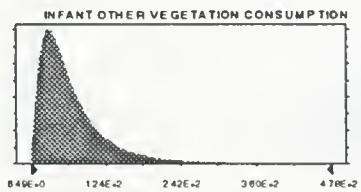
Assumption: TODDLER WATER CONSUMPTION **Cell: H29**



Assumption: INFANT ROOT VEGETABLE CONSUMPTION **Cell: E31**

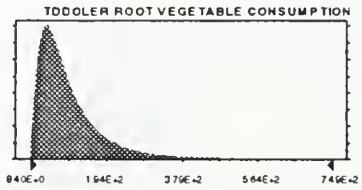


Assumption: INFANT OTHER VEGETATION CONSUMPTION **Cell: E32**



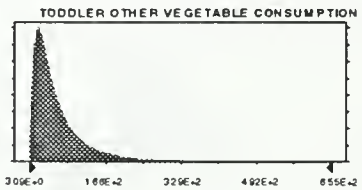
Assumption: TODDLER ROOT VEGETABLE CONSUMPTION

Cell: H31



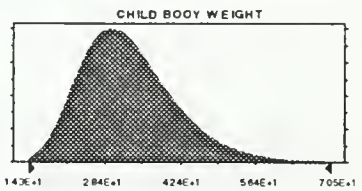
Assumption: TODDLER OTHER VEGETABLE CONSUMPTION

Cell: H32



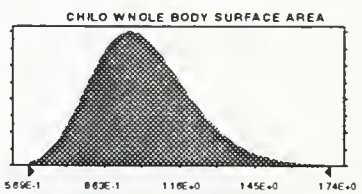
Assumption: CHILD BODY WEIGHT

Cell: K9

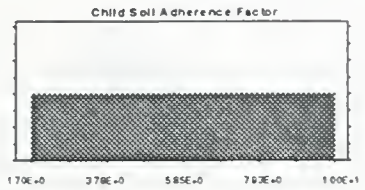


Assumption: CHILD WHOLE BODY SURFACE AREA

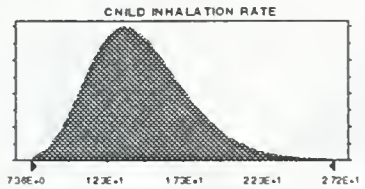
Cell: K12



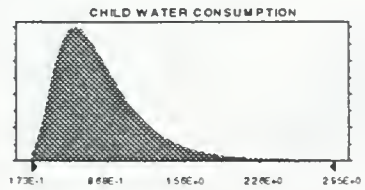
Assumption: Child Soil Adherence Factor Cell: K13



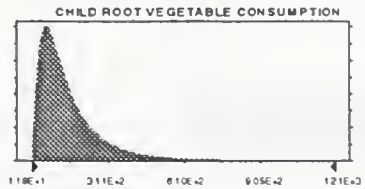
Assumption: CHILD INHALATION RATE Cell: K17



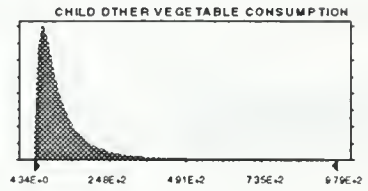
Assumption: CHILD WATER CONSUMPTION Cell: K29



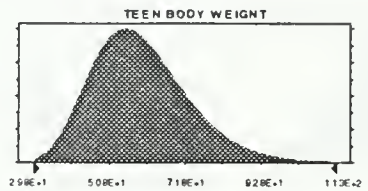
Assumption: CHILD ROOT VEGETABLE CONSUMPTION Cell: K31



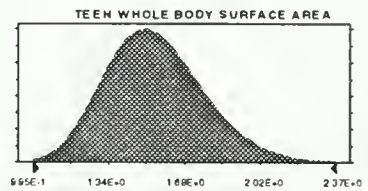
Assumption: CHILD OTHER VEGETABLE CONSUMPTION **Cell: K32**



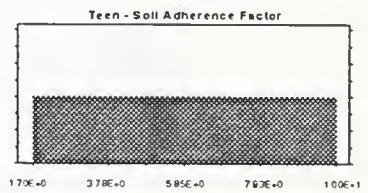
Assumption: TEEN BODY WEIGHT **Cell: N9**



Assumption: TEEN WHOLE BODY SURFACE AREA **Cell: N12**

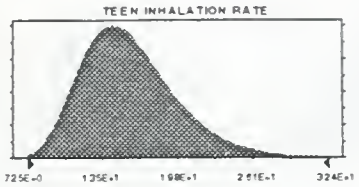


Assumption: Teen - Soil Adherence Factor **Cell: N13**



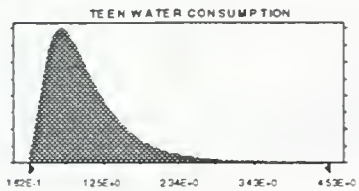
Assumption: TEEN INHALATION RATE

Cell: N17



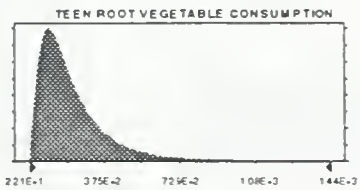
Assumption: TEEN WATER CONSUMPTION

Cell: N29



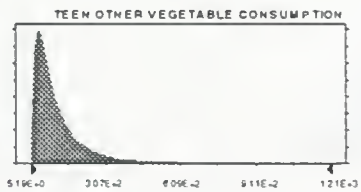
Assumption: TEEN ROOT VEGETABLE CONSUMPTION

Cell: N31



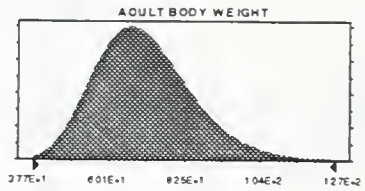
Assumption: TEEN OTHER VEGETABLE CONSUMPTION

Cell: N32



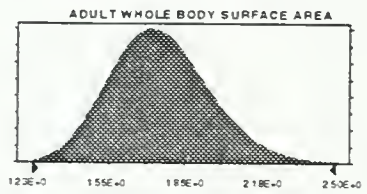
Assumption: ADULT BODY WEIGHT

Cell: Q9



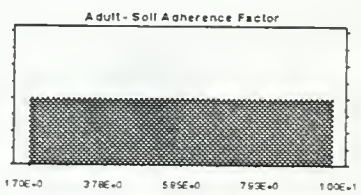
Assumption: ADULT WHOLE BODY SURFACE AREA

Cell: Q12



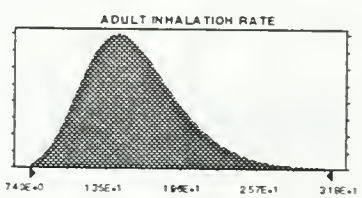
Assumption: Adult - Soil Adherence Factor

Cell: Q13

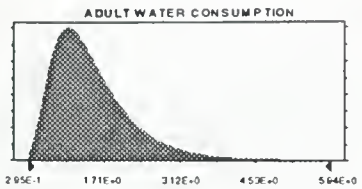


Assumption: ADULT INHALATION RATE

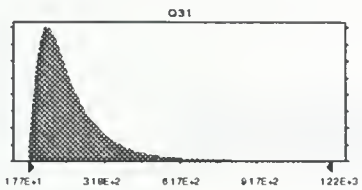
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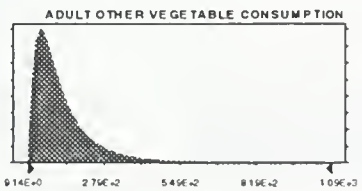
Assumption: ADULT WATER CONSUMPTION **Cell: Q29**



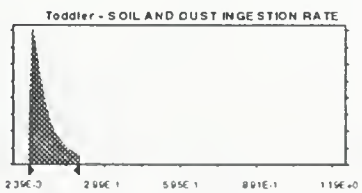
Assumption: Q31 **Cell: Q31**



Assumption: ADULT OTHER VEGETABLE CONSUMPTION **Cell: Q32**

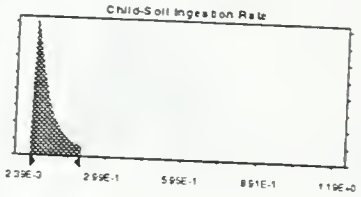


Assumption: Toddler - SOIL AND DUST INGESTION RATE **Cell: H14**



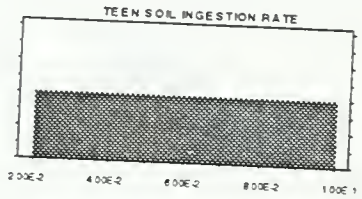
Assumption: Child-Soil Ingestion Rate

Cell: K14



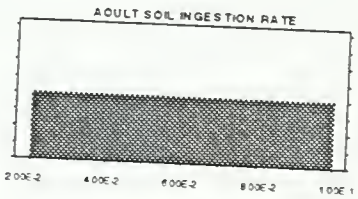
Assumption: TEEN SOIL INGESTION RATE

Cell: N14



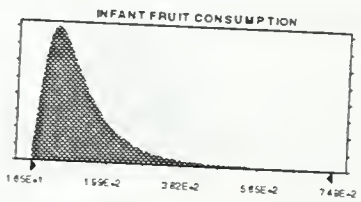
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Cell: Q14

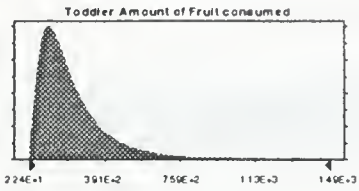


Assumption: INFANT FRUIT CONSUMPTION

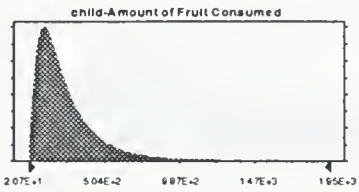
Cell: E30



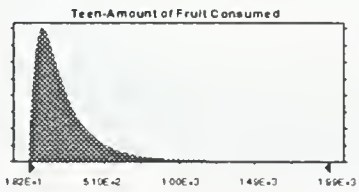
Assumption: Toddler Amount of Fruit consumed **Cell: H30**



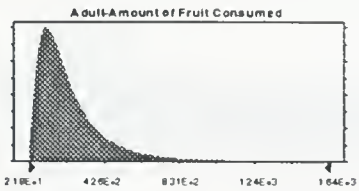
Assumption: child-Amount of Fruit Consumed **Cell: K30**



Assumption: Teen-Amount of Fruit Consumed **Cell: N30**

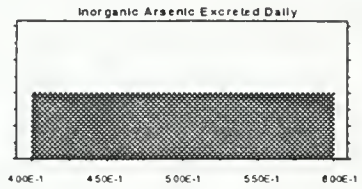


Assumption: Adult-Amount of Fruit Consumed **Cell: Q30**



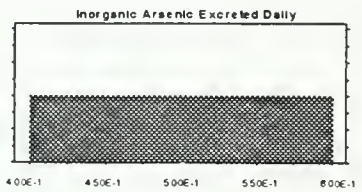
Assumption: Inorganic Arsenic Excreted Daily

Cell: E34



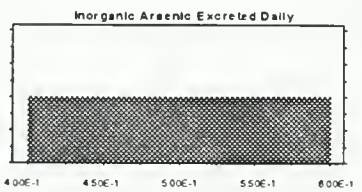
Assumption: Inorganic Arsenic Excreted Daily

Cell: H34



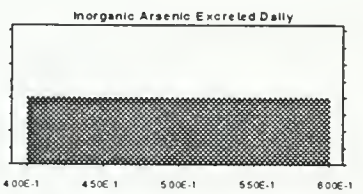
Assumption: Inorganic Arsenic Excreted Daily

Cell: K34

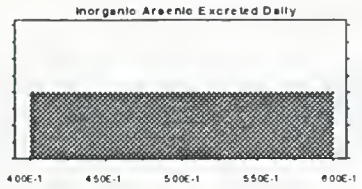


Assumption: Inorganic Arsenic Excreted Daily

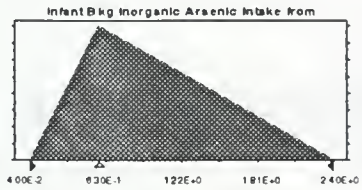
Cell: N34



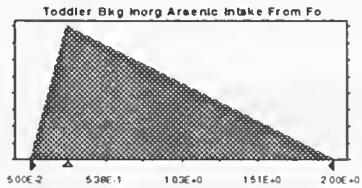
Assumption: Inorganic Arsenic Excreted Daily **Cell: Q34**



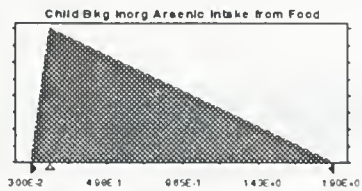
Assumption: Infant Bkg Inorganic Arsenic Intake from **Cell: E57**



Assumption: Toddler Bkg Inorg Arsenic Intake From Fo **Cell: H57**

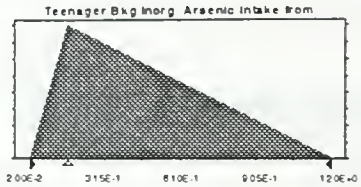


Assumption: Child Bkg Inorg Arsenic Intake from Food **Cell: K57**



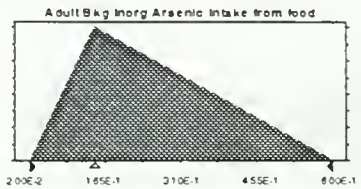
Assumption: Teenager Bkg Inorg. Arsenic intake from

Cell: N57



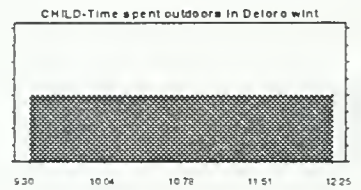
Assumption: Adult Bkg Inorg Arsenic Intake from food

Cell: Q57



Assumption: CHILD-Time spent outdoors in Deloro wint

Cell: K18

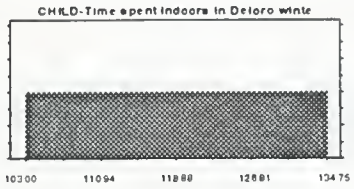


Assumption: CHILD-Time spent outdoors in Deloro summ

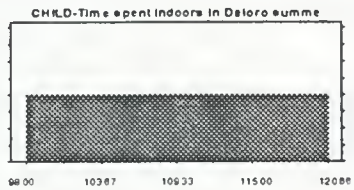
Cell: K19



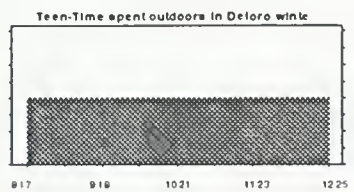
Assumption: CHILD-Time spent indoors in Deloro winte **Cell: K20**



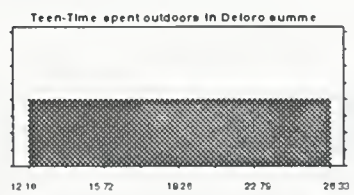
Assumption: CHILD-Time spent indoors in Deloro summe **Cell: K21**



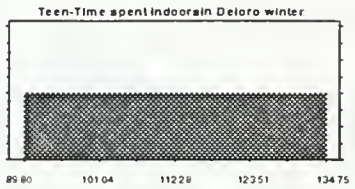
Assumption: Teen-Time spent outdoors in Deloro winte **Cell: N18**



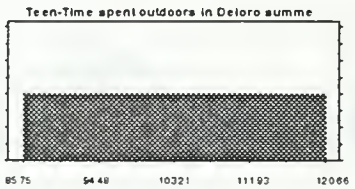
Assumption: Teen-Time spent outdoors in Deloro summe **Cell: N19**



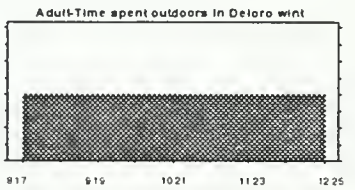
Assumption: Teen-Time spent indoorsin Deloro winter **Cell: N20**



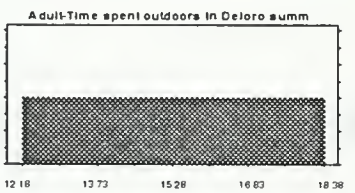
Assumption: Teen-Time spent outdoors in Deloro summe **Cell: N21**



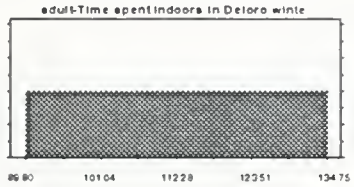
Assumption: Adult-Time spent outdoors in Deloro wint **Cell: Q18**



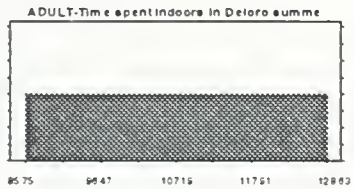
Assumption: Adult-Time spent outdoors in Deloro summ **Cell: Q19**



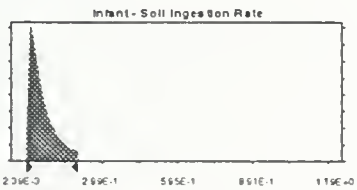
Assumption: adult-Time spent indoors in Deloro winte Cell: Q20



Assumption: ADULT-Time spent indoors in Deloro summe Cell: Q21



Assumption: Infant - Soil ingestion Rate Cell: E14



End of Assumptions

CANTOX ENVIRONMENTAL

DELORO VILLAGE
EXPOSURE ASSESSMENT AND HEALTH RISK CHARACTERIZATION FOR ARSENIC AND OTHER METALS

APPENDIX B - ENVIRONMENTAL CONCENTRATION DATA

December, 1999

TABLE B-1 SOIL CONCENTRATIONS (January 5, 1999)

	Arsenic (ppm)	Barium (ppm)	Cobalt (ppm)	Copper (ppm)	Lead (ppm)	Nickel (ppm)	Silver (ppm)
WHOLE TOWN							
minimum	2.4	46	5.1	6	3.5	8.85	0
maximum	605	405	340	115	655	195	20.5
median	78	150	41.75	24.25	95.25	34.75	2.45
mean	111.20486	162.8125	57.33056	29	121.8576	44.29063	3.733333
95th Percentile	307.75	284.25	155	57.275	344.25	101.625	9.755
standard deviation	103.28975	70.34649	53.20212	17.46038	116.7105	30.49193	3.580212
mode	170	110	20	17.5	105	11	0.3
Zone 1							
minimum	2.4	71.5	5.1	8	3.5	11	0.1
maximum	53	375	35.5	38	160	29.5	2.45
median	20.5	140	12.75	14.25	17.75	18.5	0.325
mean	26.6	172.9286	16.20357	17	43.96429	20.03571	0.585714
95th Percentile	49.75	345	31	33.75	150	29.25	1.8
mode	#N/A	150	12.5	11	#N/A	11	0.2
standard deviation	15.620302	88.99	8.51	8.75	52.26	6.01	0.64
Zone 2							
minimum	2.85	53	7.4	9	8	11	0.05
maximum	112	260	150	43.5	465	65	8.4
median	45.75	117.5	21	17.25	22	24.25	1.05
mean	46.36875	126.8906	26.93906	18.70313	52.26563	25.60938	1.492
95th Percentile	82.8	202.25	65	39.425	130.75	43.875	4.8675
mode	25	110	21	17.5	15.5	25.5	0.4
standard deviation	27.170963	46.29738	27.34494	8.709	83.97446	11.01519	1.745
Zone 3							
minimum	5.75	46	5.45	6	6.5	8.85	0
maximum	605	405	340	115	655	195	13
median	127.5	167.5	61.5	32.75	135	49.75	4.15
mean	139.78587	170.3696	71.21413	34.41304	159.5707	52.91685	4.75
95th Percentile	301.75	282.25	155.45	66.95	412	103.125	9.9125
mode	170	170	31	37	180	24.5	8.55
standard deviation	104.70662	66.99963	52.28434	18.57944	119.6415	30.90127	3.25
Zone 4							
minimum	44.5	69.5	20	10	45.5	16.5	1.25
maximum	415	385	270	48.5	220	140	20.5
median	220.75	222.5	74	29.5	80.5	60	5.28
mean	216.16667	214.9167	102.5	28.92	96.5	68.25	7.51
95th Percentile	395	357.5	241.25	45.5	189.125	131.25	18.25
mode	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	1.25
standard deviation	161.93538	115.4082	99.96	13.95	63.48	50.46	7.74

TABLE B-2 OUTDOOR AIR CONCENTRATIONS

		Cobalt ug/filter	Air Conc. ug/m3	Lead ug/filter	Air Conc. ug/m3	Nickel ug/filter	Air Conc. ug/m3	Silver ug/filter	Air Conc. ug/m3	Arsenic ug/filter	Air Conc. ug/m3	Uranium ug/filter	Air Conc. ug/m3
	RL	0.75		5		0.5		0.75		0.25		5	
WHOLE TOWN		min	1.24E-04	min	8.29E-04	min	8.29E-05	min	1.24E-04	min	4.21E-05	min	8.29E-04
		max	2.21E-04	max	4.04E-03	max	5.94E-04	max	2.21E-04	max	4.45E-04	max	1.48E-03
		mean	1.70E-04	mean	1.21E-03	mean	2.09E-04	mean	1.70E-04	mean	1.00E-04	mean	1.13E-03
		median	1.72E-04	median	1.15E-03	median	1.34E-04	median	1.72E-04	median	6.11E-05	median	1.14E-03
		S.D.	2.18E-05	S.D.	4.35E-04	S.D.	1.29E-04	S.D.	2.18E-05	S.D.	7.98E-05	S.D.	1.45E-04
		95th	2.03E-04	95th	1.39E-03	95th	4.86E-04	95th	2.03E-04	95th	2.45E-04	95th	1.35E-03
ZONE 1		min	1.67E-04	min	1.11E-03	min	1.11E-04	min	1.67E-04	min	5.57E-05	min	1.11E-03
		max	2.01E-04	max	4.04E-03	max	5.43E-04	max	2.01E-04	max	1.97E-04	max	1.34E-03
		mean	1.83E-04	mean	1.50E-03	mean	2.27E-04	mean	1.83E-04	mean	8.13E-05	mean	1.22E-03
		median	1.82E-04	median	1.22E-03	median	1.33E-04	median	1.82E-04	median	6.12E-05	median	1.22E-03
		S.D.	1.00E-05	S.D.	8.96E-04	S.D.	1.48E-04	S.D.	1.00E-05	S.D.	4.59E-05	S.D.	6.69E-05
		95th	1.99E-04	95th	2.83E-03	95th	4.52E-04	95th	1.99E-04	95th	1.66E-04	95th	1.33E-03
ZONE 2		min	1.45E-04	min	9.67E-04	min	9.67E-05	min	1.45E-04	min	4.84E-05	min	9.67E-04
		max	2.21E-04	max	1.48E-03	max	5.94E-04	max	2.21E-04	max	3.34E-04	max	1.48E-03
		mean	1.79E-04	mean	1.19E-03	mean	2.13E-04	mean	1.79E-04	mean	8.54E-05	mean	1.19E-03
		median	1.76E-04	median	1.17E-03	median	1.35E-04	median	1.76E-04	median	6.42E-05	median	1.17E-03
		S.D.	2.35E-05	S.D.	1.56E-04	S.D.	1.45E-04	S.D.	2.35E-05	S.D.	6.97E-05	S.D.	1.56E-04
		95th	2.09E-04	95th	1.39E-03	95th	4.33E-04	95th	2.09E-04	95th	2.12E-04	95th	1.39E-03
ZONE 3		min	1.24E-04	min	8.29E-04	min	8.29E-05	min	1.24E-04	min	4.21E-05	min	8.29E-04
		max	2.04E-04	max	2.80E-03	max	5.18E-04	max	2.04E-04	max	4.45E-04	max	1.36E-03
		mean	1.66E-04	mean	1.19E-03	mean	2.15E-04	mean	1.66E-04	mean	1.17E-04	mean	1.11E-03
		median	1.72E-04	median	1.15E-03	median	1.59E-04	median	1.72E-04	median	6.23E-05	median	1.14E-03
		S.D.	2.21E-05	S.D.	3.94E-04	S.D.	1.25E-04	S.D.	2.21E-05	S.D.	9.37E-05	S.D.	1.48E-04
		95th	1.94E-04	95th	1.43E-03	95th	4.86E-04	95th	1.94E-04	95th	2.67E-04	95th	1.30E-03
ZONE 4		min	1.41E-04	min	9.39E-04	min	9.39E-05	min	1.41E-04	min	4.70E-05	min	9.39E-04
		max	1.67E-04	max	1.12E-03	max	3.34E-04	max	1.67E-04	max	1.95E-04	max	1.12E-03
		mean	1.54E-04	mean	1.03E-03	mean	1.61E-04	mean	1.54E-04	mean	8.32E-05	mean	1.03E-03
		median	1.52E-04	median	1.02E-03	median	1.07E-04	median	1.52E-04	median	5.35E-05	median	1.02E-03
		S.D.	7.57E-06	S.D.	5.04E-05	S.D.	9.66E-05	S.D.	7.57E-06	S.D.	5.51E-05	S.D.	5.04E-05
		95th	1.66E-04	95th	1.11E-03	95th	3.29E-04	95th	1.66E-04	95th	1.83E-04	95th	1.11E-03

Table B-3 Indoor Air Analyzed for Metals
Sample media: Indoor air

	Flow	Sample Time	Volume of Air	Cobalt Filter Conc.	Cobalt Air Conc.	Cobalt House Average	Lead Filter Conc.	Lead Air Conc.	Lead House Average	Nickel Filter Conc.	Nickel Air Conc.	Nickel House Average	Silver Filter Conc.	Silver Air Conc.	Silver House Average	Arsenic Filter Conc.	Arsenic Air Conc.	Arsenic House Average	Uranium Filter Conc.	Uranium Air Conc.	Uranium House Average
	(lpm)	(min)	(m3)	ug/filter	µg/m3	ug/m3	ug/filter	µg/m3	ug/m3	ug/filter	µg/m3	ug/m3	ug/filter	µg/m3	ug/m3	ug/filter	µg/m3	ug/m3	ug/filter	µg/m3	ug/m3
RL				0 75			5.0			0 50			0.75			0 25			5 0		
WHOLE TOWN																					
Min	3 1	352	3 73	0.38	0.04	0.05	2 5	0 29	0.31	0.25	0.03	0 03	0.38	0 04	0.05	0 13	0 01	0.02	2 5	0 29	0.31
Max	15	2785	8 63	0.38	0.10	0 09	2.5	0 67	0.57	2.10	0 40	0 22	0.38	0.10	0 09	0.13	0 03	0 03	2.5	0 67	0.57
Median	3 1	1697	5 28	0 38	0 07	0.07	2.50	0 47	0 47	0.25	0 05	0.05	0.38	0 07	0 07	0.13	0 02	0 02	2.5	0 47	0 47
Mean	4 2	1597	5 44	0 38	0 07	0.07	2.5	0.47	0 47	0.27	0 05	0.05	0 38	0 07	0.07	0 13	0.02	0 02	2.5	0 47	0 47
Standard Deviation	3 43	410	0.69	0.0	0.01	0.01	0.0	0.05	0 04	0.17	0 03	0 02	0.00	0.01	0 01	0 00	0.0	0 0	0.0	0.05	0.04
ZONE 1																					
Min	3 1	1221 0	3 8	0.38	0.1	0.1	2.50	0.5	0.5	0 25	0 0	0 0	0.38	0.1	0.1	0 13	0 0	0 0	2 50	0 5	0 5
Max	3 1	1708 0	5 3	0.38	0.1	0.1	2.50	0.7	0 6	0 25	0.1	0.1	0.38	0.1	0.1	0.13	0.0	0 0	2.50	0.7	0 6
Median	3 1	1689	5 23	0.38	0	0 07	2 50	0	0.48	0 25	0	0 05	0.38	0	0 07	0 13	0	0 02	2 50	0	0 48
Mean	3.1	1639	5 08	0.38	0	0 07	2.50	0	0.50	0 25	0	0.05	0.38	0	0 07	0.13	0	0 02	2 50	0	0 50
Standard Deviation	0 00	148	0.46	0.0	0	0.01	0 0	0	0.04	0 0	0	0 00	0.0	0	0.01	0 0	0	0.00	0 0	0	0.04
ZONE 2																					
Min	3 1	540 0	4.3	0.38	0.0	0.0	2.50	0.3	0.3	0 25	0.0	0 0	0.38	0 0	0.0	0.13	0.0	0.0	2 50	0.3	0.3
Max	15	2424	8	0 38	0	0	2.50	1	1	0.25	0	0	0.38	0	0	0 13	0	0	2.50	1	1
Median	3 1	1685 0	5 3	0 38	0 1	0 1	2.50	0 5	0 5	0 25	0.0	0 0	0.38	0 1	0 1	0 13	0 0	0 0	2 50	0 5	0 5
Mean	4 4	1585 7	5 6	0.38	0.1	0.1	2.50	0 5	0 5	0 25	0.0	0.0	0.38	0 1	0 1	0.13	0.0	0.0	2.50	0 5	0 5
Standard Deviation	3 65	412 21	1 02	0 0	0 01	0 01	0 0	0 07	0 06	0 0	0.01	0.01	0 0	0.01	0.01	0 0	0 00	0 00	0 0	0 07	0 06
ZONE 3																					
Min	3 1	352 0	3.7	0 38	0 0	0.1	2 50	0.3	0 4	0 25	0 0	0 0	0.38	0 0	0 1	0 13	0 0	0 0	2 50	0 3	0 4
Max	15	2785	9	0 38	0	0	2.50	1	1	2 10	0	0	0 38	0	0	0 13	0	0	2 50	1	1
Median	3.1	1710 0	5 3	0 38	0 1	0.1	2.50	0.5	0 5	0 25	0 0	0 0	0 38	0 1	0.1	0 13	0 0	0 0	2 50	0 5	0 5
Mean	3 8	1652.1	5.4	0.38	0.1	0.1	2.50	0.5	0 5	0 28	0.1	0.1	0.38	0.1	0.1	0 13	0.0	0 0	2.50	0 5	0 5
Standard Deviation	2 78	364 37	0 57	0 0	0 01	0.00	0.0	0.05	0 03	0 2	0.04	0.03	0.0	0.01	0 00	0 0	0.00	0 00	0 0	0 05	0 03
ZONE 4																					
Min	3 1	1682.0	5.2	0 38	0 1	0.1	2 50	0.5	0 5	0 25	0 0	0.0	0.38	0.1	0.1	0 13	0.0	0.0	2 50	0 5	0 5
Max	3	1699	5	0.38	0	0	2.50	0	0	0 25	0	0	0 38	0	0	0 13	0	0	2 50	0	0
Median	3 1	1692.0	5 2	0 38	0 1	0.1	2 50	0.5	0.5	0 25	0.0	0 0	0.38	0.1	0.1	0.13	0 0	0 0	2 50	0 5	0 5
Mean	3 1	1691.3	5 2	0.38	0 1	0.1	2.50	0 5	0 5	0.25	0.0	0.0	0.38	0.1	0.1	0.13	0.0	0.0	2.50	0.5	0.5
Standard Deviation	0 00	8 10	0 03	0.0	0 00	0 00	0 0	0 00	0 00	0.0	0.00	0 00	0 0	0 00	0 00	0.0	0 00	0 00	0 0	0 00	0 00

Table B-4 Deloro Drinking Water Wells (first draw) Metals Analysis

Sample Media: Groundwater
Sampled: October 14, 1998

	Study ID	Cobalt mg/L	Lead mg/L	Nickel mg/L	Silver mg/L	Arsenic mg/L	Uranium mg/L
RL		0.05	0.0006	0.01	0.00005	0.005	0.10
	br	<	<	<	<	<	<
	bs	<	<	<	<	<	<
	bt	<	<	<	<	<	<
	bu	<	0.0031	<	<	<	<
	bv	<	0.018	<	0.00024	<	<
	bw	<	0.25	0.01	<	<	<
	by	<	0.0079	<	<	<	<
	bb	<	<	<	<	<	<
	bf	<	<	<	<	<	<
	bh	<	<	<	<	<	<
	bi	<	<	<	<	<	<
	bl	<	<	<	0.00014	<	<
	bm	<	0.0044	<	<	<	<
	bn	<	0.0083	<	<	<	<
	c	<	<	<	<	<	<
QA/QC							
Metal duplicate	bb	<	<	<	<	<	<
min		0.025	0.0003	0.005	0.000025	0.0025	0.05
max		0.025	0.25	0.01	0.00024	0.0025	0.05
median		0.025	0.0003	0.005	0.000025	0.0025	0.05
mean		0.025	0.019627	0.005333	0.000047	0.0025	0.05
standard deviation		0	0.063923	0.001291	6.11E-05	0	0
ODWO							
MAC	mg/L		0.01				0.1
IMAC	mg/L					0.025	
Proposed (1996)	mg/L					0.010	
GUCS	mg/L	0.1	0.01	0.1	0.0012	0.025	

Note:

RL	Laboratory reporting limit
<	Less than RL
ODWO	Ontario Drinking Water Objectives, Table 1-Chemical/Physical Objectives, revised 1994
GUCS	Guideline for Use at Contaminated Sites in Ontario, Table A for a Potable Groundwater Condition, revised 1997
Proposed (1996)	Draft - Rationale Document for the Development of Soil, Drinking Water, Surface Water, and Air Quality Criteria for Arsenic, February 1996, Standards Development Branck, OMOE
MAC	Maximum Acceptable Concentration
IMAC	Interim Maximum Acceptable Concentration

For calculation purposes, 0.5*RL used for all sample concentrations less than RL
min, max, mean, and std. dev does not include duplicate

min	0.025	0.0003	0.005	0.000025	0.0025	0.05
max	0.025	0.25	0.01	0.00024	0.0025	0.05
median	0.025	0.0031	0.005	0.000025	0.0025	0.05
mean	0.025	0.04	0.0057	5.57E-05	0.0025	0.05
standard deviation	3.80E-10	9.28E-02	1.89E-03	8.13E-05	0.00E+00	7.60E-10

min	0.025	0.0003	0.005	0.000025	0.0025	0.05
max	0.025	0.0083	0.005	0.00014	0.0025	0.05
median	0.025	0.0003	0.005	0.000025	0.0025	0.05
mean	0.025	0.002029	0.005	4.14E-05	0.0025	0.05
standard deviation	3.80E-10	3.16E-03	0.00E+00	4.35E-05	0.00E+00	7.60E-10

Table B-5 Deloro Drinking Water Wells (flushed) Metals Analysis

Sample Media: Groundwater
All wells sampled October 14/98 except replicate (October 15/98)

Sample ID	Study ID	Cobalt mg/L	Lead mg/L	Nickel mg/L	Silver mg/L	Arsenic mg/L	Uranium mg/L
RL		0.05	0.0006	0.01	0.00005	0.005	0.10
	br	<	<	<	0.00011	<	<
	bs	<	<	<	<	<	<
	bt	<	<	<	<	<	<
	bu	<	<	<	<	<	<
	bv	<	<	<	<	<	<
	bw	<	<	<	<	<	<
	by	<	0.0068	<	<	<	<
	bb	<	<	<	<	<	<
	bf	<	<	<	<	<	<
	bh	<	<	<	<	<	<
	bi	<	<	<	0.00011	<	<
	bl	<	<	<	<	<	<
	bm	<	<	<	0.00012	<	<
	bn	<	<	<	<	<	<
	c	<	<	<	<	<	<
QA/QC							
24-hour replicate	bl	<	<	<	<	<	<
Trip blank		<	<	<	<	<	<
Min		0.025	0.0003	0.005	0.000025	0.0025	0.05
Max		0.025	0.0068	0.005	0.00012	0.0025	0.05
Median		0.025	0.0003	0.005	0.000025	0.0025	0.05
Mean		0.025	0.000733	0.005	4.27E-05	0.0025	0.05
Standard Deviation		0	0.001678	0	3.66E-05	0	0
ODWO							
MAC	mg/L		0.01				0.1
IMAC	mg/L					0.025	
Proposed (1996)	mg/L					0.010	
GUCS	mg/L	0.1	0.01	0.1	0.0012	0.025	

Note:

RL	Laboratory reporting limit
ODWO	Ontario Drinking Water Objectives, Table 1 Chemical/Physical Objectives, revised 1994.
GUCS	Guideline for Use at Contaminated Sites in Ontario, Table A for a potable groundwater condition, revised Fe
Proposed (1996)	Draft - Rationale Document for the Development of Soil, Drinking Water, Surface Water, and Air Quality Crit for Arsenic, February 1996, Standards Development Branck, OMOE
MAC	Maximum Acceptable Concentration
IMAC	Interim Maximum Acceptable Concentration

Tap flushed for 5 minutes before sample collected.
For calculation purposes, 0.5*RL used for all sample concentrations less than RL
min, max, mean and std. dev. does not include duplicates or blanks

Min	0.025	0.0003	0.005	0.000025	0.0025	0.05
Max	0.025	0.0068	0.005	0.00011	0.0025	0.05
Median	0.025	0.0003	0.005	0.000025	0.0025	0.05
Mean	0.025	0.001229	0.005	3.71E-05	0.0025	0.05
Standard Deviation	3.80E-10	2.46E-03	0.00E+00	3.21E-05	0.00E+00	7.60E-10

Min	0.025	0.0003	0.005	0.000025	0.0025	0.05
Max	0.025	0.0003	0.005	0.00012	0.0025	0.05
Median	0.025	0.0003	0.005	0.000025	0.0025	0.05
Mean	0.025	0.0003	0.005	5.07E-05	0.0025	0.05
Standard Deviation	3.80E-10	0.00E+00	0.00E+00	4.40E-05	0.00E+00	7.60E-10

TABLE B-6 DELORO MUNICIPAL WELL

PARAMETER	UNITS	Sampling Date		ODWO Criteria			GUCS
		1994 17-May OCWA	1998 14-Apr OCWA	MAC	IMAC	Proposed (1996)	
arsenic	mg/L	0.0051	<0.01		0.025	0.010	0.025
cobalt	mg/L	<0.00002	<0.004				0.1
lead	mg/L	0.00007<T	<0.002	0.01			0.01
nickel	mg/L	<0.0002	<0.01				0.1
silver	mg/L	<0.00005	-				0.0012
uranium	mg/L	0.00026<T	<0.1	0.1			

Notes:

- = not analyzed
<T = a measurable trace amount, interpret with caution

ODWO	Ontario Drinking Water Objectives, Table 1 Chemical/Physical Objectives, revised 1994.
GUCS	Guideline for Use at Contaminated Sites in Ontario, Table A for a potable groundwater condition, revised February 1997
Proposed (1996)	Draft - Rationale Document for the Development of Soil, Drinking Water, Surface Water, and Air Quality Criteria for Arsenic, February 1996, Standards Development Branck, OMOE
MAC	Maximum Acceptable Concentration
IMAC	Interim Maximum Acceptable Concentration

Table B-7 Outdoor Dustfall analyzed for Metals
Sample media: Dust

	Cobalt		Lead		Nickel		Silver		Arsenic		Uranium	
	ug/container	ug/100cm2 /30 days	ug/container	ug/100cm2 /30 days	ug/container	ug/100cm2 /30 days	ug/container	ug/100cm2 /30 days	ug/container	ug/100cm2 /30 days	ug/container	ug/100cm2 /30 days
RL	0.75		5.0		0.50		0.75		0.25		5.0	
WHOLE TOWN												
min	0.75	0.41	5	2.74	0.5	0.27	0.75	0.41	0.25	0.14	5	2.74
max	4	2.19	26.5	14.54	2.65	1.45	4	2.19	2.9	1.59	26.5	14.54
mean	2.23	1.22	14.8	8.13	1.49	0.82	2.23	1.22	1.16	0.64	14.81	8.13
median	2.33	1.28	15.75	8.64	1.625	0.89	2.325	1.28	1.075	0.59	15.75	8.64
standard deviation	1.21	0.67	8.10	4.44	0.81	0.45	1.21	0.67	0.78	0.43	8.10	4.44
Zone 2												
min	2.3	1.26	15.5	8.50	1.65	0.91	2.3	1.26	0.75	0.41	15.5	8.50
max	3.4	1.87	22.5	12.34	2.25	1.23	3.4	1.87	1.15	0.63	22.5	12.34
mean	2.85	1.56	19.00	10.42	1.95	1.07	2.85	1.56	0.95	0.52	19.00	10.42
median	2.85	1.56	19.00	10.42	1.95	1.07	2.85	1.56	0.95	0.52	19.00	10.42
standard deviation	0.78	0.43	4.95	2.72	0.42	0.23	0.78	0.43	0.28	0.16	4.95	2.72
Zone 3												
min	1	0.55	6.5	3.57	0.65	0.36	1	0.55	1	0.55	6.5	3.57
max	4	2.19	26.5	14.54	2.65	1.45	4	2.19	2.9	1.59	26.5	14.54
mean	2.25	1.23	14.88	8.16	1.49	0.82	2.25	1.23	1.60	0.88	14.88	8.16
median	2.00	1.10	13.25	7.27	1.33	0.73	2.00	1.10	1.25	0.69	13.25	7.27
standard deviation	1.50	0.82	10.03	5.50	1.00	0.55	1.50	0.82	0.88	0.48	10.03	5.50

Table B-8 Indoor Dustfall - Corrected for 30 days and 100 cm2

	Number of Days	Cobalt		Lead		Nickel		Silver		Arsenic		Uranium	
		ug/dish	ug/100cm2 /30 days	ug/dish	ug/100cm2 /30 days	ug/dish	ug/100cm2 /30 days	ug/dish	ug/100cm2 /30 days	ug/dish	ug/100cm2 /30 days	ug/dish	ug/100cm2 /30 days
RL		0.75		5.0		0.50		0.75		0.25		5.0	
WHOLE TOWN													
Min	24.0	0.38	0.20	2.5	1.32	0.25	0.13	0.38	0.20	0.13	0.07	2.5	1.32
Max	37.0	0.38	0.30	21.0	12.78	72.0	48.37	0.38	0.30	0.13	0.10	2.5	2.03
Median	32.0	0.38	0.23	2.5	1.52	0.25	0.15	0.38	0.23	0.13	0.08	2.5	1.52
Mean	31.3	0.38	0.23	3.2	1.97	2.7	1.75	0.38	0.23	0.13	0.08	2.5	1.56
Standard Deviati	2.0	0.00	0.02	2.8	1.72	10.9	7.21	0.00	0.02	0.00	0.01	0	0.11
ZONE 1													
Min	24.000	0.375	0.228	2.500	1.522	0.250	0.152	0.375	0.228	0.125	0.076	2.500	1.522
Max	32.000	0.375	0.304	2.500	2.029	2.200	1.382	0.375	0.304	0.125	0.101	2.500	2.029
Median	32.000	0.375	0.228	2.500	1.522	0.250	0.152	0.375	0.228	0.125	0.076	2.500	1.522
Mean	30.875	0.375	0.239	2.500	1.591	0.650	0.407	0.375	0.239	0.125	0.080	2.500	1.591
Standard Deviati	2.7999	0.0000	0.0267	0.0000	0.1777	0.7639	0.4742	0.0000	0.0267	0.0000	0.0089	0.0000	0.1777
ZONE 2													
Min	28.000	0.375	0.221	2.500	1.476	0.250	0.148	0.375	0.221	0.125	0.074	2.500	1.476
Max	33.000	0.375	0.261	2.500	1.739	2.900	1.712	0.375	0.261	0.125	0.087	2.500	1.739
Median	32.000	0.375	0.228	2.500	1.522	0.250	0.163	0.375	0.228	0.125	0.076	2.500	1.522
Mean	31.000	0.375	0.237	2.500	1.578	0.740	0.456	0.375	0.237	0.125	0.079	2.500	1.578
Standard Deviati	2.1602	0.0000	0.0172	0.0000	0.1149	1.0373	0.6260	0.0000	0.0172	0.0000	0.0057	0.0000	0.1149
ZONE 3													
Min	28.000	0.375	0.197	2.500	1.316	0.250	0.132	0.375	0.197	0.125	0.066	2.500	1.316
Max	37.000	0.375	0.261	21.000	12.784	72.000	48.365	0.375	0.261	0.125	0.087	2.500	1.739
Median	32.000	0.375	0.228	2.500	1.522	0.250	0.152	0.375	0.228	0.125	0.076	2.500	1.522
Mean	31.500	0.375	0.233	3.514	2.182	3.789	2.464	0.375	0.233	0.125	0.078	2.500	1.551
Standard Deviati	1.8283	0.0000	0.0139	3.4592	2.1260	13.5184	8.9491	0.0000	0.0139	0.0000	0.0046	0.0000	0.0925

Table B-9 Metal Analysis of Dust on Roads and Exterior Surfaces

Sample media: Dust

Location	Cobalt µg/100cm²	Lead µg/100cm²	Nickel µg/100cm²	Silver µg/100cm²	Arsenic µg/100cm²	Uranium µg/100cm²	Cobalt µg/100cm²	Lead µg/100cm²	Nickel µg/100cm²	Silver µg/100cm²	Arsenic µg/100cm²	Uranium µg/100cm²
RL	0.75	5.0	0.50	0.75	0.25	5.0	0.75	5.0	0.50	0.75	0.25	5.0
WHOLE TOWN												
Min	0.38	2.5	1.8	0.38	0.38	2.5	0.38	2.5	0.25	0.38	0.13	2.5
Max	6	11	19	0.38	16	9.3	4.8	1700	15	0.38	83	2.5
Median	1.6	8.5	12	0.38	2.5	2.5	0.38	202	1.02	0.38	0.55	2.5
Mean	2.1	7.3	10.5	0.38	4.9	4.57	1.34	422.2	3.31	0.38	12.31	2.5
Standard de	1.89	3.47	6.63	0.0	5.59	2.77	1.82	577.6	5.10	0.0	28.85	0.0
Zone 2												
Min	0.38	2.5	1.8	0.38	0.38	2.5	0.38	9.8	0.25	0.38	0.13	2.5
Max	2.8	9.2	12	0.38	8.8	2.5	3.7	680	15	0.38	0.97	2.5
Median	1.59	5.85	6.9	0.38	4.59	2.5	2.04	344.9	7.63	0.38	0.55	2.5
Mean	1.59	5.85	6.9	0.38	4.59	2.5	2.04	344.9	7.63	0.38	0.55	2.5
Standard de	1.71	4.74	7.21	0.0	5.95	0.0	2.35	473.9	10.43	0.0	0.6	0.0
Zone 3												
Min	1.1	3.9	5	0.38	1.9	2.5	0.4	51	0.3	0.4	0.1	2.5
Max	1.9	11	19	0.4	3.1	6.5	4.8	1700	5.9	0.4	83	2.5
Median	1.6	5	16	0.38	2.5	2.5	0.4	202	1	0.4	1.1	2.5
Mean	1.53	6.63	13.33	0.38	2.5	3.83	1.48	538.75	2.05	0.38	21.31	2.5
Standard de	0.4	3.82	7.37	0.0	0.6	2.31	2.21	786.77	2.6	0.0	41.13	0.0

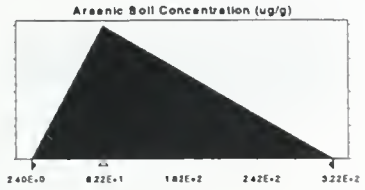
Table B-10 Indoor Swipes Analyzed for Metals												
Sampled media: Dust												
	Cobalt		Lead		Nickel		Silver		Arsenic		Uranium	
	ug/100 cm2	Household averages	ug/100 cm2	Household averages	ug/100 cm2	Household averages	ug/100 cm2	Household averages	ug/100 cm2	Household averages	ug/100 cm2	Household averages
RL	0.75		5.0		0.50		0.75		0.25		5.0	
WHOLE TOWN												
Min	0.375	0.38	2.5	2.5	0.25	0.25	0.375	0.38	0.125	0.13	2.5	2.5
Max	1.8	1.09	130	66.3	4.3	2.65	3.7	2.04	2.5	1.54	2.5	2.5
Median	0.375	0.38	2.5	2.50	0.8	0.84	0.375	0.38	0.125	0.13	2.5	2.5
Mean	0.41	0.41	5.26	5.3	0.99	0.99	0.40	0.40	0.29	0.29	2.5	2.5
Standard Deviation	0.19	0.13	13.02	9.3	0.76	0.58	0.31	0.22	0.44	0.33	0.0	0.0
Zone 1												
Min	0.375	0.38	2.5	2.50	0.25	0.25	0.375	0.38	0.125	0.13	2.5	2.50
Max	0.375	0.38	2.5	2.50	3.1	2.65	0.375	0.38	1.9	1.01	2.5	2.50
Median	0.375	0.38	2.5	2.50	0.95	1.35	0.375	0.38	0.125	0.13	2.5	2.50
Mean	0.375	0.38	2.5	2.50	1.21	1.21	0.375	0.38	0.236	0.24	2.5	2.50
Standard Deviation	0	0	0	0	0.98	0.824	0	0	0.444	0.314	0	0
Zone 2												
Min	0.375	0.38	2.5	2.50	0.25	0.25	0.375	0.38	0.125	0.13	2.5	2.50
Max	0.375	0.38	2.5	2.50	3	2.05	3.7	2.04	2.3	1.54	2.5	2.50
Median	0.375	0.38	2.5	2.50	0.68	0.71	0.375	0.38	0.125	0.13	2.5	2.50
Mean	0.375	0.38	2.5	2.50	0.8945	0.89	0.54125	0.54	0.266	0.27	2.5	2.50
Standard Deviation	0	0	0	0	0.743	0.544	0.743	0.526	0.500	0.446	0	0
Zone 3												
Min	0.375	0.38	2.5	2.50	0.25	0.25	0.375	0.38	0.125	0.13	2.5	2.50
Max	1.8	1.09	130	66.25	4.3	2.50	0.375	0.38	2.5	1.31	2.5	2.50
Median	0.375	0.38	2.5	2.50	0.805	0.85	0.375	0.38	0.125	0.13	2.5	2.50
Mean	0.433	0.43	6.793	6.79	0.980	0.98	0.375	0.38	0.319	0.32	2.5	2.50
Standard Deviation	0.229	0.158	16.072	11.391	0.725	0.545	0	0	0.433	0.311	0	0
Zone 4												
Min	0.375	0.38	2.5	2.50	0.25	0.50	0.375	0.38	0.125	0.13	2.5	2.50
Max	0.375	0.38	2.5	2.50	1	0.84	0.375	0.38	0.125	0.13	2.5	2.50
Median	0.375	0.38	2.5	2.50	0.71	0.67	0.375	0.38	0.125	0.13	2.5	2.50
Mean	0.375	0.38	2.5	2.50	0.6675	0.67	0.375	0.38	0.125	0.13	2.5	2.50
Standard Deviation	0	0	0	0	0.312	0.237	0	0	0	0	0	0

Assumptions (Distributions)

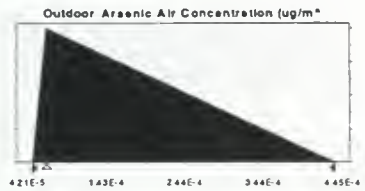
Probabilistic Chemical Concentrations for Whole Town and Background

WHOLE TOWN-ARSENIC

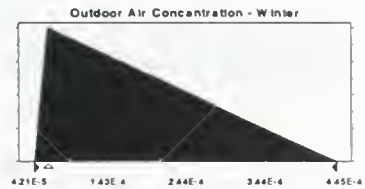
Assumption: Arsenic Soil Concentration (ug/g) Cell: G11



Assumption: Outdoor Arsenic Air Concentration (ug/m^3) Cell: G12



Assumption: Outdoor Air Concentration - Winter Cell: G13

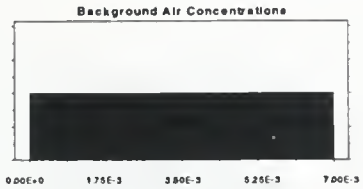


Assumption: Background Soil Concentrations Cell: D11

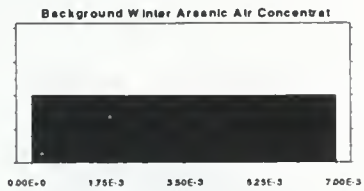


WHOLE TOWN-ARSENIC

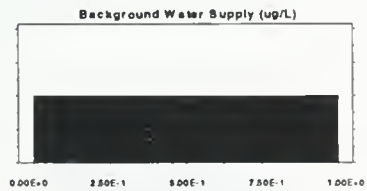
Assumption: Background Air Concentrations Cell: D12



Assumption: Background Winter Arsenic Air Concentrat Cell: D13



Assumption: Background Water Supply (ug/L) Cell: D23



Note: Assumptions are presented for the Whole Town only. Data to characterize assumtion: each zone are presented in Tables B-1 through B-10. These assumptions or distributions characterizing the zones will be similar to those for the Whole Town.

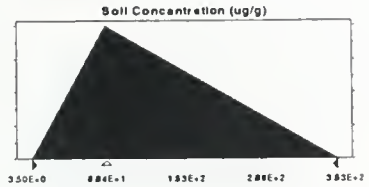
End of Assumptions

Assumptions (Distributions)

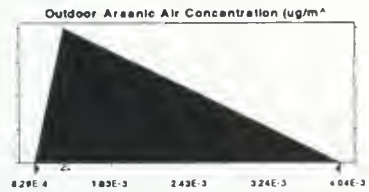
Probabilistic Chemical Concentrations for Whole Town and Background

WHOLE TOWN-LEAD

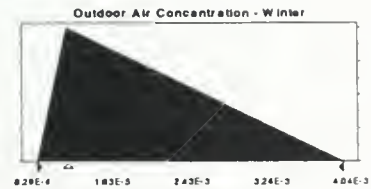
Assumption: Soil Concentration (ug/g) Cell: G9



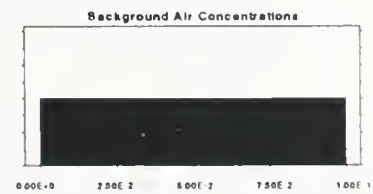
Assumption: Outdoor Air Concentration (ug/m^3) Cell: G10



Assumption: Outdoor Air Concentration - Winter Cell: G11



Assumption: Background Air Concentrations Cell: D10



Assumption: Background Winter Air Concentrat Cell: D11

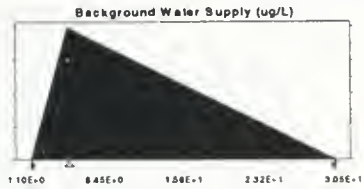




WHOLE TOWN-LEAD

Assumption: Background Water Supply (ug/L)

Cell: D21



Note: Assumptions are presented for the Whole Town only. Data to characterize assumtion: each zone are presented in Tables B-1 through B-10. These assumptions or distributions characterizing the zones will be similar to those for the Whole Town.

End of Assumptions

CANTOX ENVIRONMENTAL

DELORO VILLAGE
EXPOSURE ASSESSMENT AND HEALTH RISK CHARACTERIZATION FOR ARSENIC AND OTHER METALS

APPENDIX C - DETAILED RESULTS

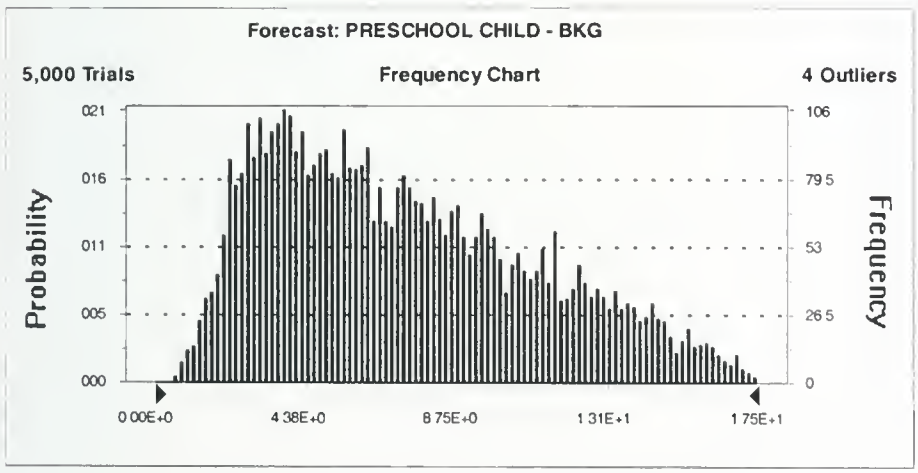
December, 1999

NON-CANCER ARSENIC RISKS

HOME PRODUCE CONSUMPTION - WHOLE TOWN

Forecast: PRESCHOOL CHILD - BKG

Statistics:	Value
Trials	5000
Mean	7.21E+00
Median	6.57E+00
Mode	---
Standard Deviation	3.85E+00
Variance	1.48E+01
Skewness	0.54
Kurtosis	2.40
Coeff. of Variability	0.53
Range Minimum	6.14E-01
Range Maximum	1.84E+01
Range Width	1.78E+01
Mean Std. Error	5.45E-02



Forecast: PRESCHOOL CHILD - BKG (cont'd)

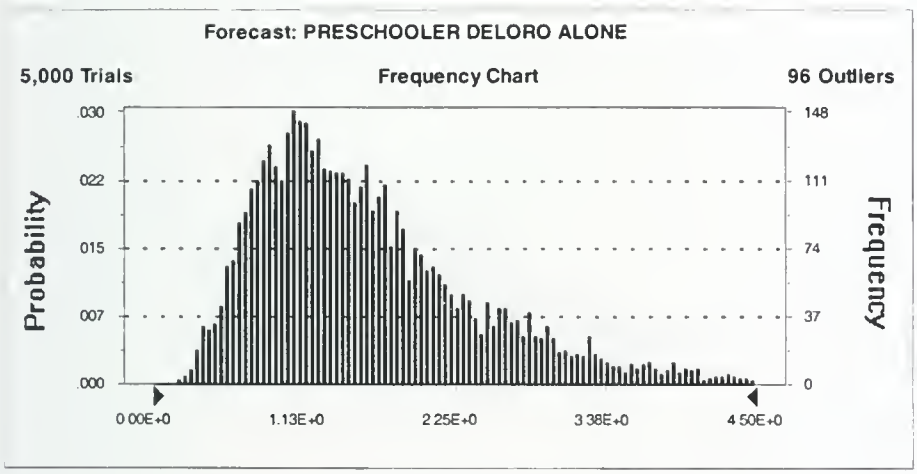
Percentiles:

Percentile	Value
0.0%	6.14E-01
2.5%	1.73E+00
5.0%	2.15E+00
50.0%	6.57E+00
95.0%	1.44E+01
97.5%	1.55E+01
100.0%	1.84E+01

End of Forecast

Forecast: PRESCHOOLER DELORO ALONE

Statistics:	Value
Trials	5000
Mean	1.68E+00
Median	1.45E+00
Mode	---
Standard Deviation	9.82E-01
Variance	9.64E-01
Skewness	1.98
Kurtosis	10.71
Coeff. of Variability	0.59
Range Minimum	1.83E-01
Range Maximum	1.18E+01
Range Width	1.16E+01
Mean Std. Error	1.39E-02



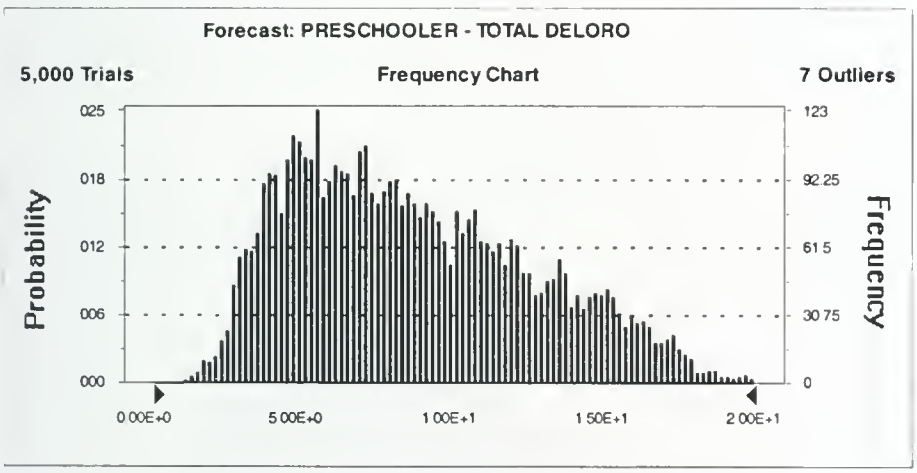
Percentiles:

Percentile	Value
0.0%	1.83E-01
2.5%	4.87E-01
5.0%	5.93E-01
50.0%	1.45E+00
95.0%	3.53E+00
97.5%	4.21E+00
100.0%	1.18E+01

End of Forecast

Forecast: PRESCHOOLER - TOTAL DELORO

Statistics:	Value
Trials	5000
Mean	8.65E+00
Median	8.05E+00
Mode	---
Standard Deviation	3.99E+00
Variance	1.59E+01
Skewness	0.51
Kurtosis	2.47
Coeff. of Variability	0.46
Range Minimum	1.16E+00
Range Maximum	2.48E+01
Range Width	2.36E+01
Mean Std. Error	5.64E-02



Percentiles:

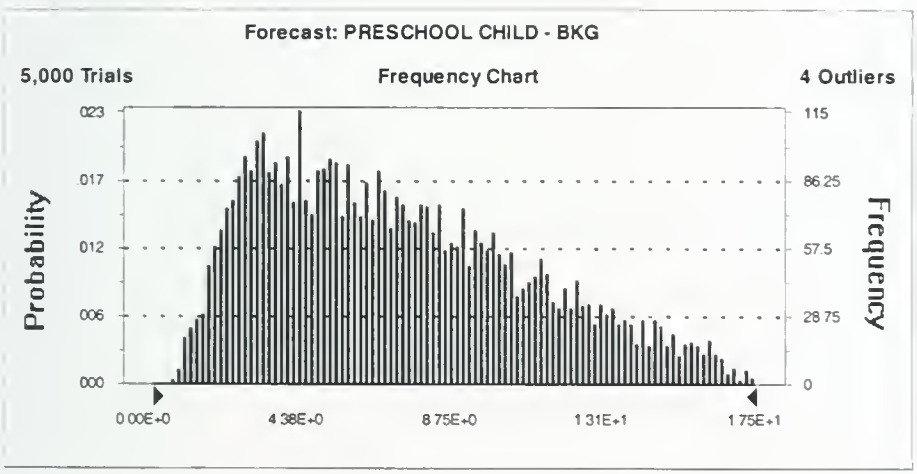
Percentile	Value
0.0%	1.16E+00
2.5%	2.79E+00
5.0%	3.25E+00
50.0%	8.05E+00
95.0%	1.60E+01
97.5%	1.70E+01
100.0%	2.48E+01

End of Forecast

NON-CANCER ARSENIC RISKS - WHOLE TOWN
NO HOME GARDEN PRODUCE CONSUMPTION

Forecast: PRESCHOOL CHILD - BKG

Statistics:	Value
Trials	5000
Mean	7.13E+00
Median	6.55E+00
Mode	---
Standard Deviation	3.82E+00
Variance	1.46E+01
Skewness	0.54
Kurtosis	2.45
Coeff. of Variability	0.54
Range Minimum	6.14E-01
Range Maximum	1.78E+01
Range Width	1.72E+01
Mean Std. Error	5.41E-02



Forecast: PRESCHOOL CHILD - BKG (cont'd)

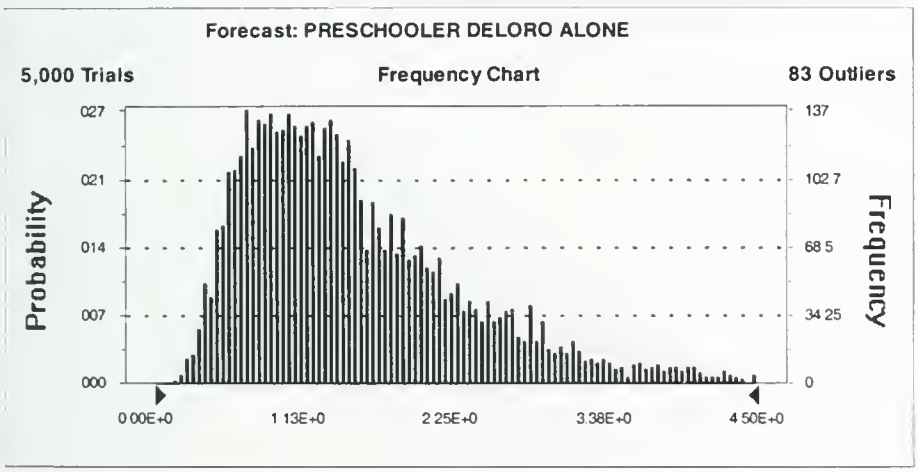
Percentiles:

Percentile	Value
0.0%	6.14E-01
2.5%	1.64E+00
5.0%	2.02E+00
50.0%	6.55E+00
95.0%	1.44E+01
97.5%	1.55E+01
100.0%	1.78E+01

End of Forecast

Forecast: PRESCHOOLER DELORO ALONE

Statistics:	Value
Trials	5000
Mean	1.56E+00
Median	1.33E+00
Mode	---
Standard Deviation	9.91E-01
Variance	9.82E-01
Skewness	2.57
Kurtosis	18.30
Coeff. of Variability	0.64
Range Minimum	1.71E-01
Range Maximum	1.42E+01
Range Width	1.41E+01
Mean Std. Error	1.40E-02



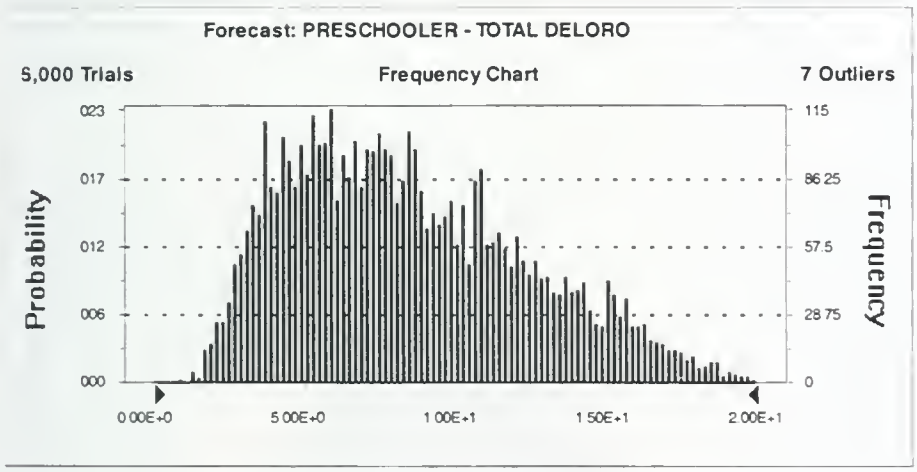
Percentiles:

Percentile	Value
0.0%	1.71E-01
2.5%	4.26E-01
5.0%	5.07E-01
50.0%	1.33E+00
95.0%	3.30E+00
97.5%	4.00E+00
100.0%	1.42E+01

End of Forecast

Forecast: PRESCHOOLER - TOTAL DELORO

Statistics:	Value
Trials	5000
Mean	8.48E+00
Median	7.89E+00
Mode	---
Standard Deviation	3.96E+00
Variance	1.57E+01
Skewness	0.56
Kurtosis	2.72
Coeff. of Variability	0.47
Range Minimum	9.80E-01
Range Maximum	2.80E+01
Range Width	2.70E+01
Mean Std. Error	5.60E-02



Percentiles:

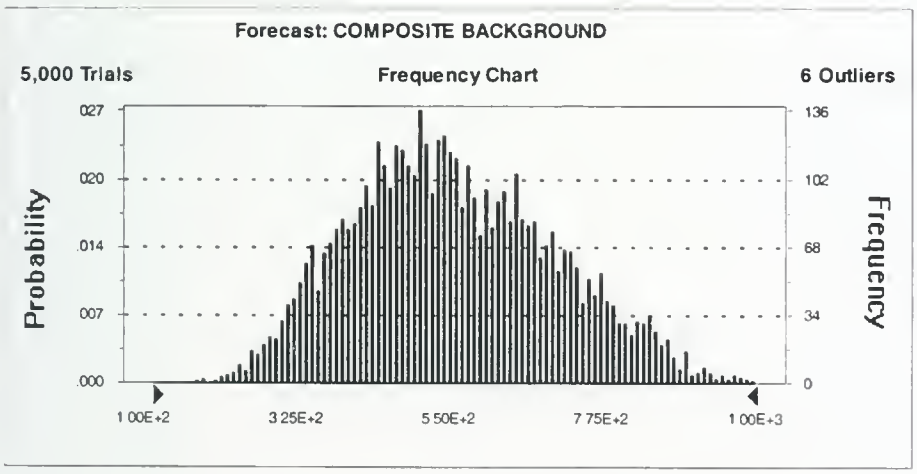
Percentile	Value
0.0%	9.80E-01
2.5%	2.61E+00
5.0%	3.06E+00
50.0%	7.89E+00
95.0%	1.58E+01
97.5%	1.69E+01
100.0%	2.80E+01

End of Forecast

CANCER RISK LEVELS ASSOCIATED WITH ARSENIC - WHOLE TOWN
HOME GARDEN PRODUCE

Forecast: COMPOSITE BACKGROUND

Statistics:	Value
Trials	5000
Mean	5.49E+02
Median	5.37E+02
Mode	---
Standard Deviation	1.51E+02
Variance	2.29E+04
Skewness	0.29
Kurtosis	2.60
Coeff. of Variability	0.28
Range Minimum	1.65E+02
Range Maximum	1.10E+03
Range Width	9.37E+02
Mean Std. Error	2.14E+00

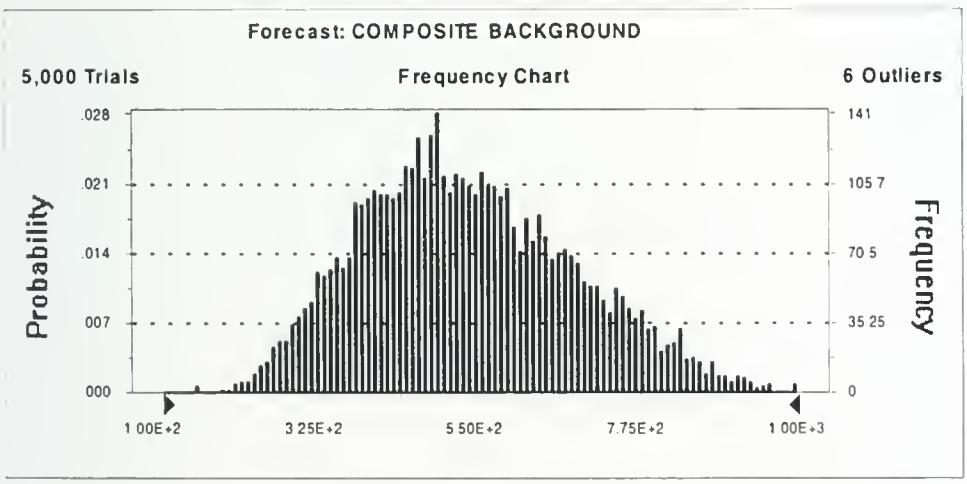


CANCER RISK LEVLES ASSOCIATED WITH ARSENIC VIA ORAL AND DER

WHOLE TOWN

Forecast: COMPOSITE BACKGROUND **Cell: B55**

Statistics:	Value
Trials	5000
Mean	5.34E+02
Median	5.20E+02
Mode	---
Standard Deviation	1.52E+02
Variance	2.31E+04
Skewness	0.35
Kurtosis	2.71
Coeff. of Variability	0.28
Range Minimum	1.38E+02
Range Maximum	1.09E+03
Range Width	9.49E+02
Mean Std. Error	2.15E+00



Forecast: COMPOSITE BACKGROUND (cont'd) **Cell: B55**

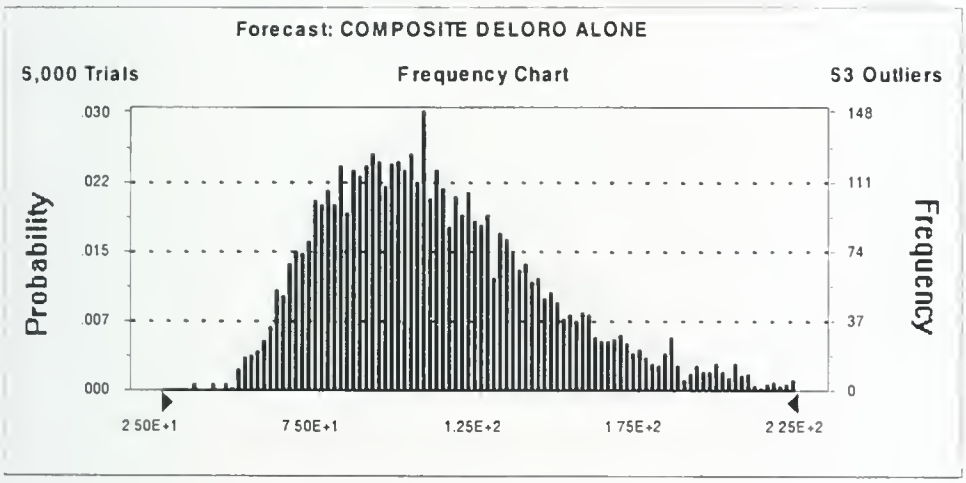
Percentiles:

Percentile	Value
0.0%	1.38E+02
2.5%	2.74E+02
5.0%	3.04E+02
50.0%	5.20E+02
95.0%	8.02E+02
97.5%	8.50E+02
100.0%	1.09E+03

End of Forecast

Forecast: COMPOSITE DELORO ALONE **Cell: C55**

Statistics:	Value
Trials	5000
Mean	1.13E+02
Median	1.07E+02
Mode	---
Standard Deviation	3.72E+01
Variance	1.38E+03
Skewness	1.11
Kurtosis	5.33
Coeff. of Variability	0.33
Range Minimum	3.06E+01
Range Maximum	3.79E+02
Range Width	3.49E+02
Mean Std. Error	5.25E-01



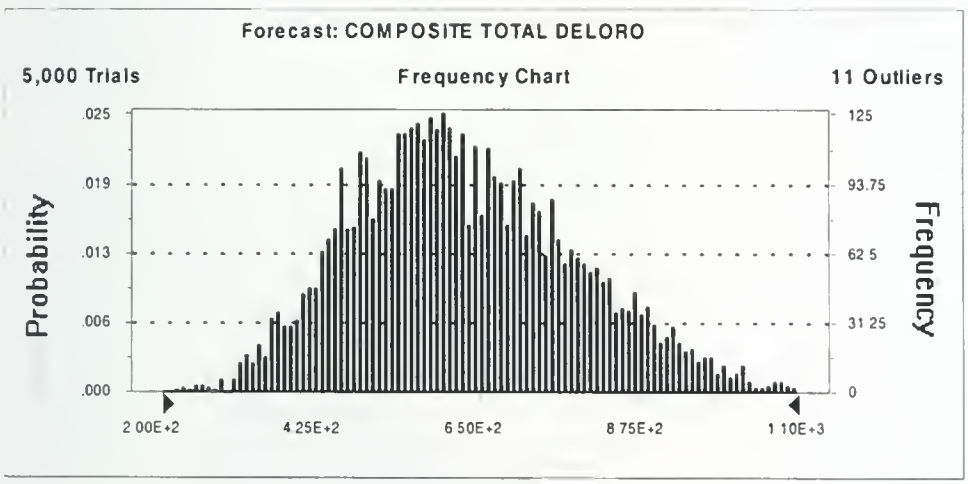
Percentiles:

Percentile	Value
0.0%	3.06E+01
2.5%	6.00E+01
5.0%	6.48E+01
50.0%	1.07E+02
95.0%	1.83E+02
97.5%	2.02E+02
100.0%	3.79E+02

End of Forecast

Forecast: COMPOSITE TOTAL DELORO **Cell: D55**

Statistics:	Value
Trials	5000
Mean	6.30E+02
Median	6.14E+02
Mode	---
Standard Deviation	1.57E+02
Variance	2.47E+04
Skewness	0.36
Kurtosis	2.81
Coeff. of Variability	0.25
Range Minimum	1.97E+02
Range Maximum	1.25E+03
Range Width	1.05E+03
Mean Std. Error	2.22E+00



Percentiles:

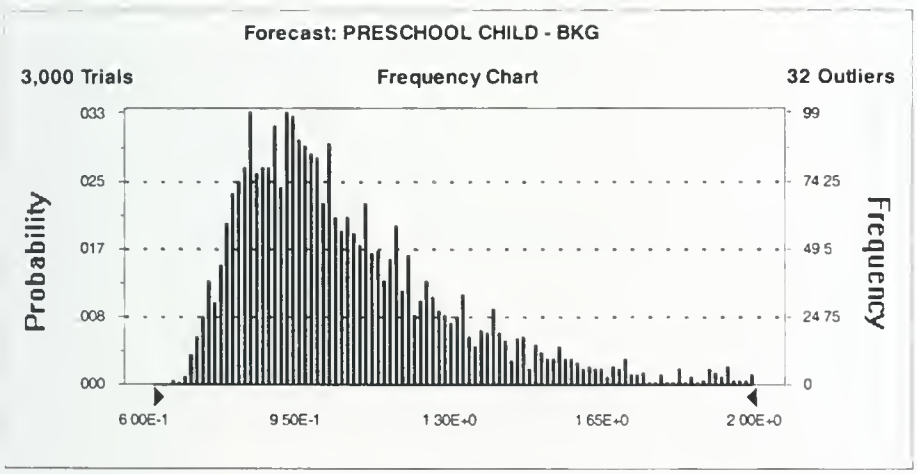
Percentile	Value
0.0%	1.97E+02
2.5%	3.58E+02
5.0%	3.92E+02
50.0%	6.14E+02
95.0%	9.10E+02
97.5%	9.61E+02
100.0%	1.25E+03

End of Forecast

Preschool Child Risk Estimates
Home Garden Produce Consumer

Forecast: PRESCHOOL CHILD - Typical Onatrio Resident **Cell: B16**

Statistics:	Value
Trials	3000
Mean	1.07E+00
Median	9.93E-01
Mode	---
Standard Deviation	2.90E-01
Variance	8.41E-02
Skewness	2.40
Kurtosis	14.96
Coeff. of Variability	0.27
Range Minimum	6.50E-01
Range Maximum	4.11E+00
Range Width	3.45E+00
Mean Std. Error	5.30E-03



Forecast: PRESCHOOL CHILD - BKG (cont'd) **Cell: B16**

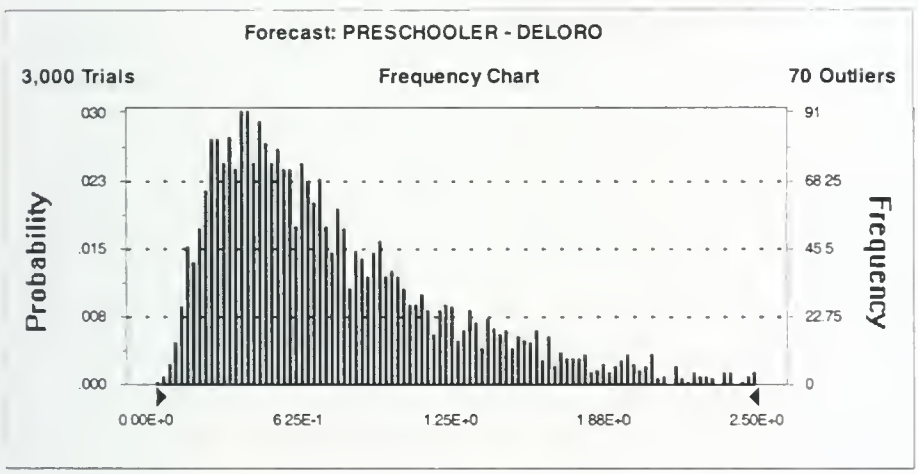
Percentiles:

Percentile	Value
0.0%	6.50E-01
2.5%	7.32E-01
5.0%	7.61E-01
50.0%	9.93E-01
95.0%	1.59E+00
97.5%	1.82E+00
100.0%	4.11E+00

End of Forecast

Forecast: PRESCHOOLER - DELORO ALONE **Cell: C16**

Statistics:	Value
Trials	3000
Mean	8.00E-01
Median	6.26E-01
Mode	---
Standard Deviation	6.52E-01
Variance	4.25E-01
Skewness	2.73
Kurtosis	15.68
Coeff. of Variability	0.81
Range Minimum	2.24E-02
Range Maximum	6.55E+00
Range Width	6.53E+00
Mean Std. Error	1.19E-02



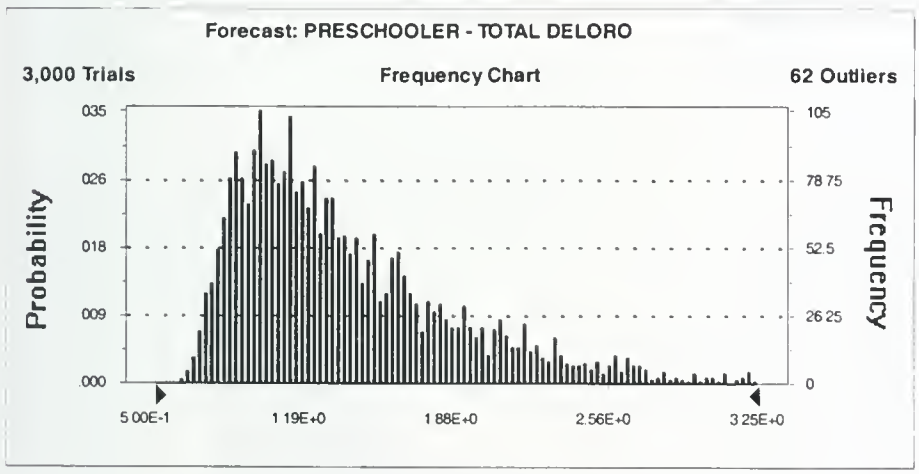
Percentiles:

Percentile	Value
0.0%	2.24E-02
2.5%	1.38E-01
5.0%	1.81E-01
50.0%	6.26E-01
95.0%	1.95E+00
97.5%	2.46E+00
100.0%	6.55E+00

End of Forecast

Forecast: PRESCHOOLER - TOTAL DELORO **Cell: D16**

Statistics:	Value
Trials	3000
Mean	1.43E+00
Median	1.25E+00
Mode	---
Standard Deviation	6.62E-01
Variance	4.38E-01
Skewness	2.68
Kurtosis	15.26
Coeff. of Variability	0.46
Range Minimum	6.20E-01
Range Maximum	7.15E+00
Range Width	6.53E+00
Mean Std. Error	1.21E-02



Percentiles:

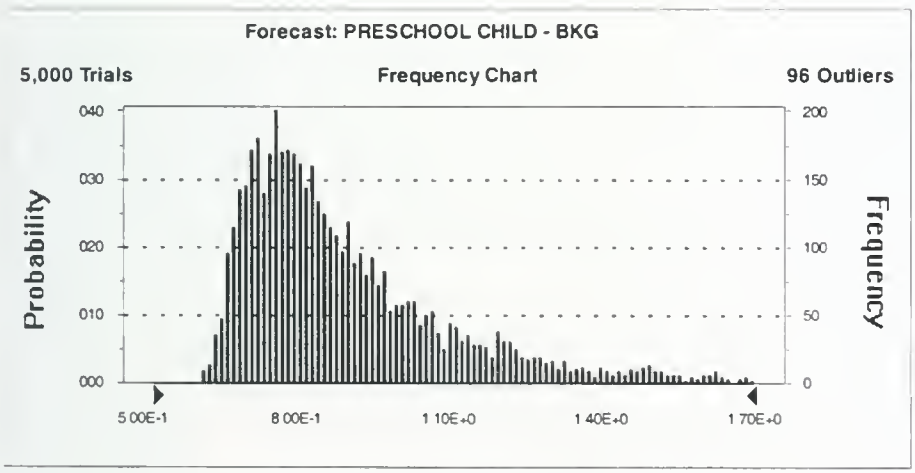
Percentile	Value
0.0%	6.20E-01
2.5%	7.51E-01
5.0%	7.98E-01
50.0%	1.25E+00
95.0%	2.59E+00
97.5%	3.09E+00
100.0%	7.15E+00

End of Forecast

Preschool Child Exposure Ratios
Non Home Garden Consumer

Forecast: PRESCHOOL CHILD - Typical Ontario **Cell: B16**

Statistics:	Value
Trials	5000
Mean	9.09E-01
Median	8.30E-01
Mode	---
Standard Deviation	2.76E-01
Variance	7.63E-02
Skewness	3.10
Kurtosis	20.24
Coeff. of Variability	0.30
Range Minimum	5.97E-01
Range Maximum	4.14E+00
Range Width	3.55E+00
Mean Std. Error	3.91E-03



Forecast: PRESCHOOL CHILD - Typical Ontario (cont'd) **Cell: B16**

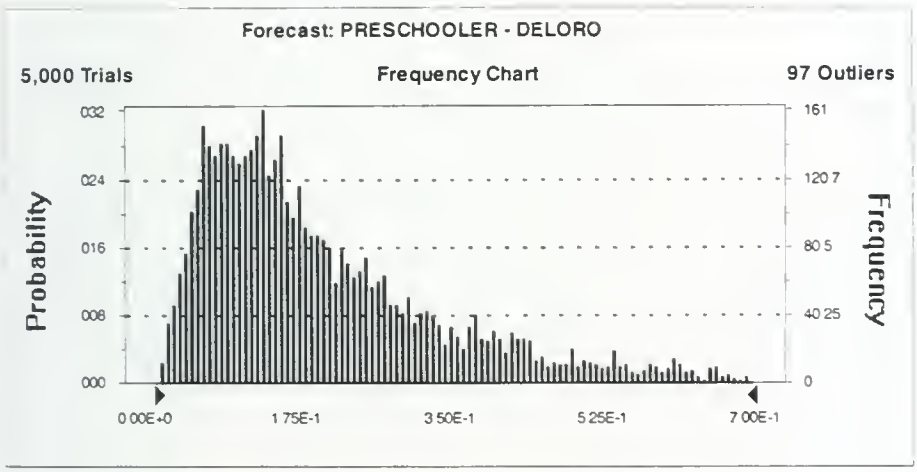
Percentiles:

Percentile	Value
0.0%	5.97E-01
2.5%	6.47E-01
5.0%	6.61E-01
50.0%	8.30E-01
95.0%	1.43E+00
97.5%	1.62E+00
100.0%	4.14E+00

End of Forecast

Forecast: PRESCHOOLER - DELORO ALONE Cell: C16

Statistics:	Value
Trials	5000
Mean	2.10E-01
Median	1.60E-01
Mode	---
Standard Deviation	1.67E-01
Variance	2.77E-02
Skewness	1.93
Kurtosis	8.50
Coeff. of Variability	0.79
Range Minimum	8.45E-03
Range Maximum	1.46E+00
Range Width	1.45E+00
Mean Std. Error	2.36E-03



Percentiles:

Percentile	Value
0.0%	8.45E-03
2.5%	3.15E-02
5.0%	4.28E-02
50.0%	1.60E-01
95.0%	5.45E-01
97.5%	6.52E-01
100.0%	1.46E+00

End of Forecast

Forecast: COMPOSITE BACKGROUND (cont'd)

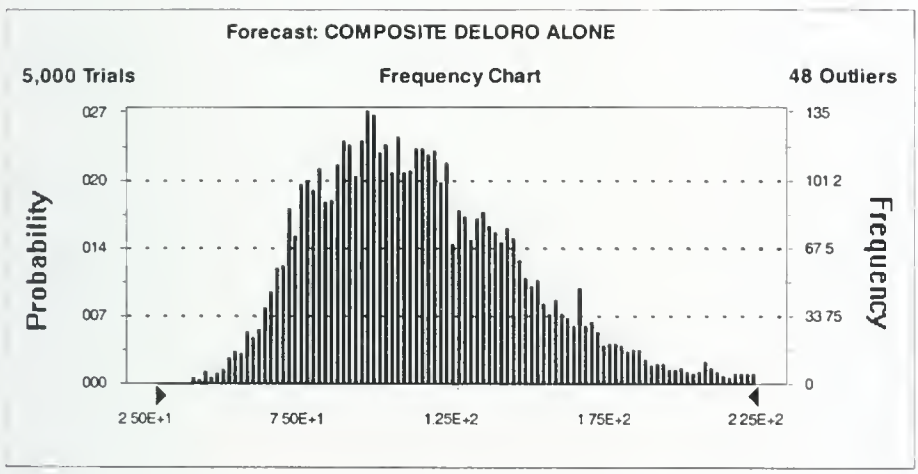
Percentiles:

Percentile	Value
0.0%	1.65E+02
2.5%	2.88E+02
5.0%	3.19E+02
50.0%	5.37E+02
95.0%	8.17E+02
97.5%	8.54E+02
100.0%	1.10E+03

End of Forecast

Forecast: COMPOSITE DELORO ALONE

Statistics:	Value
Trials	5000
Mean	1.14E+02
Median	1.09E+02
Mode	---
Standard Deviation	3.62E+01
Variance	1.31E+03
Skewness	0.98
Kurtosis	4.83
Coeff. of Variability	0.32
Range Minimum	3.73E+01
Range Maximum	3.50E+02
Range Width	3.13E+02
Mean Std. Error	5.12E-01



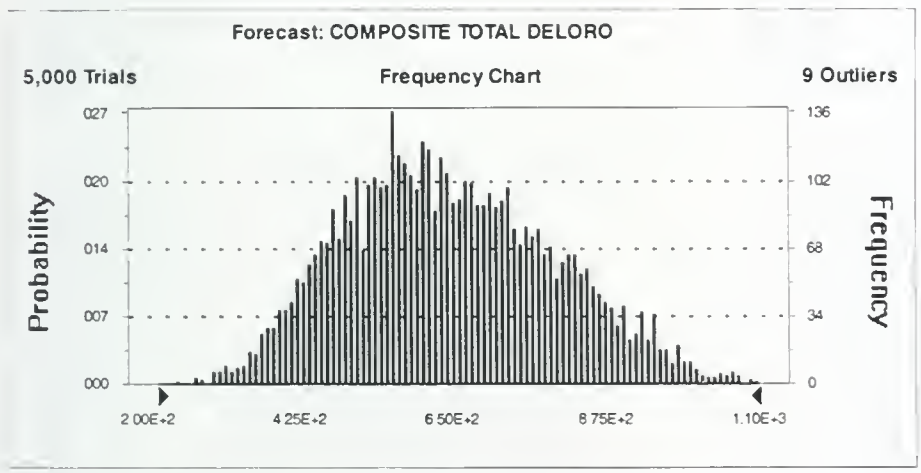
Percentiles:

Percentile	Value
0.0%	3.73E+01
2.5%	5.92E+01
5.0%	6.57E+01
50.0%	1.09E+02
95.0%	1.79E+02
97.5%	1.99E+02
100.0%	3.50E+02

End of Forecast

Forecast: COMPOSITE TOTAL DELORO

Statistics:	Value
Trials	5000
Mean	6.38E+02
Median	6.27E+02
Mode	---
Standard Deviation	1.56E+02
Variance	2.43E+04
Skewness	0.28
Kurtosis	2.61
Coeff. of Variability	0.24
Range Minimum	2.33E+02
Range Maximum	1.19E+03
Range Width	9.61E+02
Mean Std. Error	2.20E+00



Percentiles:

Percentile	Value
0.0%	2.33E+02
2.5%	3.67E+02
5.0%	4.02E+02
50.0%	6.27E+02
95.0%	9.12E+02
97.5%	9.49E+02
100.0%	1.19E+03

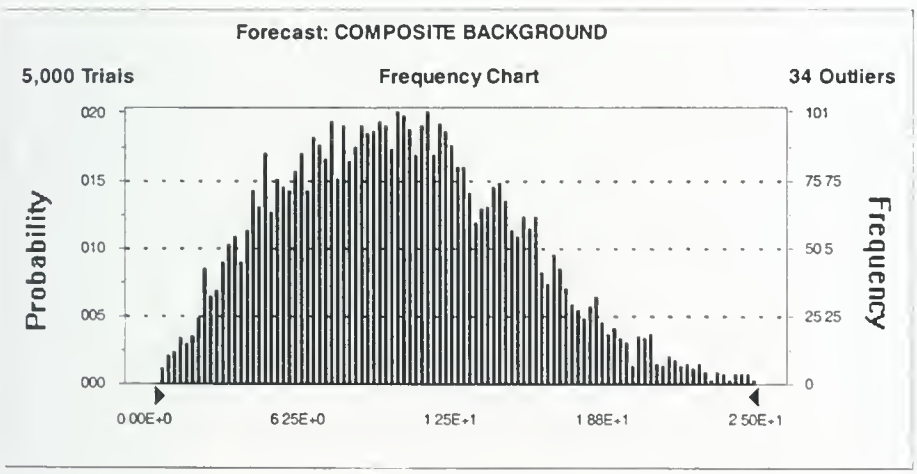
End of Forecast

CANCER RISK LEVLES ASSOCIATED WITH ARSENIC VIA INHALATION ONLY

WHOLE TOWN

Forecast: COMPOSITE BACKGROUND **Cell: B55**

Statistics:	Value
Trials	5000
Mean	1.03E+01
Median	1.00E+01
Mode	---
Standard Deviation	4.98E+00
Variance	2.48E+01
Skewness	0.51
Kurtosis	3.26
Coeff. of Variability	0.48
Range Minimum	2.86E-01
Range Maximum	3.38E+01
Range Width	3.35E+01
Mean Std. Error	7.05E-02



Forecast: COMPOSITE BACKGROUND (cont'd) **Cell: B55**

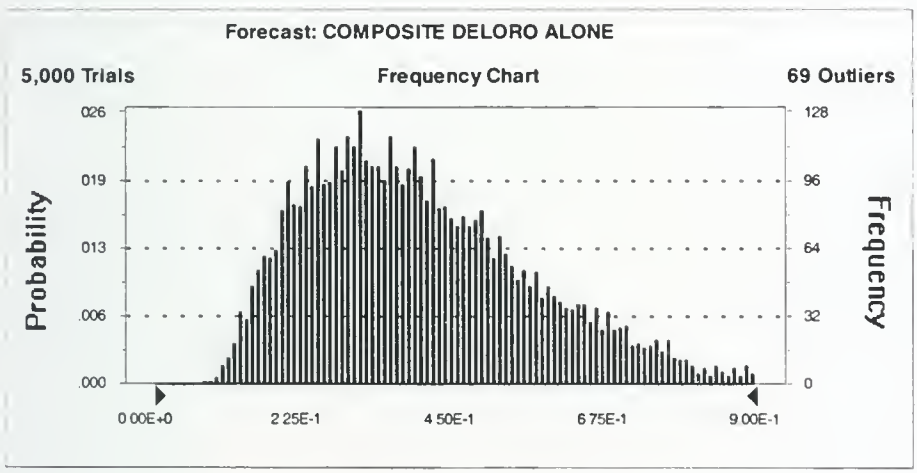
Percentiles:

Percentile	Value
0.0%	2.86E-01
2.5%	2.11E+00
5.0%	2.94E+00
50.0%	1.00E+01
95.0%	1.89E+01
97.5%	2.09E+01
100.0%	3.38E+01

End of Forecast

Forecast: COMPOSITE DELORO ALONE **Cell: C55**

Statistics:	Value
Trials	5000
Mean	4.05E-01
Median	3.76E-01
Mode	---
Standard Deviation	1.78E-01
Variance	3.17E-02
Skewness	0.87
Kurtosis	3.73
Coeff. of Variability	0.44
Range Minimum	7.76E-02
Range Maximum	1.18E+00
Range Width	1.10E+00
Mean Std. Error	2.52E-03



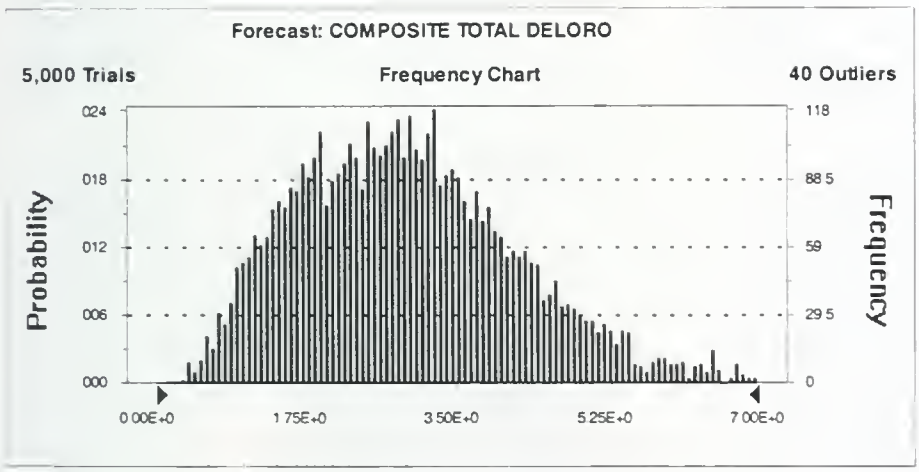
Percentiles:

Percentile	Value
0.0%	7.76E-02
2.5%	1.46E-01
5.0%	1.69E-01
50.0%	3.76E-01
95.0%	7.39E-01
97.5%	8.20E-01
100.0%	1.18E+00

End of Forecast

Forecast: COMPOSITE TOTAL DELORO **Cell: D55**

Statistics:	Value
Trials	5000
Mean	2.95E+00
Median	2.83E+00
Mode	---
Standard Deviation	1.33E+00
Variance	1.77E+00
Skewness	0.72
Kurtosis	3.89
Coeff. of Variability	0.45
Range Minimum	3.05E-01
Range Maximum	1.07E+01
Range Width	1.04E+01
Mean Std. Error	1.88E-02



Percentiles:

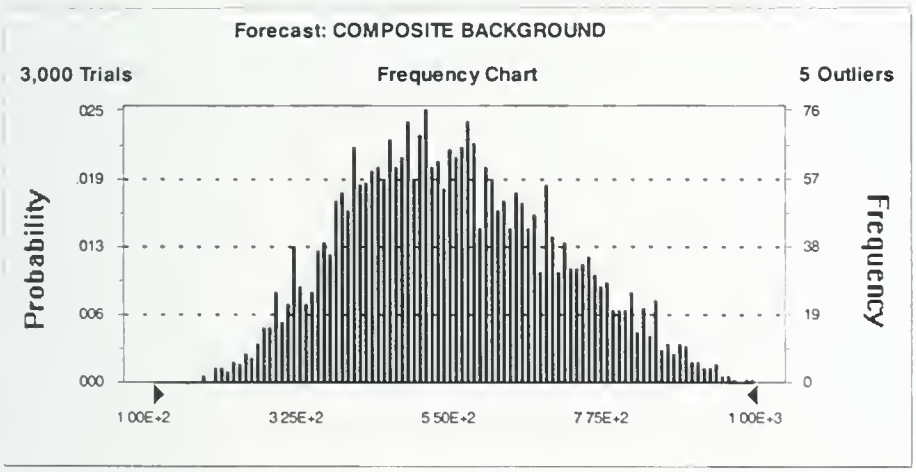
Percentile	Value
0.0%	3.05E-01
2.5%	8.67E-01
5.0%	1.04E+00
50.0%	2.83E+00
95.0%	5.28E+00
97.5%	5.95E+00
100.0%	1.07E+01

End of Forecast

CANCER RISK LEVELS ASSOCIATED WITH ARSENIC - WHOLE TOWN
NO HOME GARDEN PRODUCE CONSUMPTION

Forecast: COMPOSITE BACKGROUND **Cell: B55**

Statistics:	Value
Trials	3000
Mean	5.49E+02
Median	5.39E+02
Mode	---
Standard Deviation	1.56E+02
Variance	2.45E+04
Skewness	0.27
Kurtosis	2.59
Coeff. of Variability	0.28
Range Minimum	1.73E+02
Range Maximum	1.09E+03
Range Width	9.20E+02
Mean Std. Error	2.86E+00



Forecast: COMPOSITE BACKGROUND (cont'd) **Cell: B55**

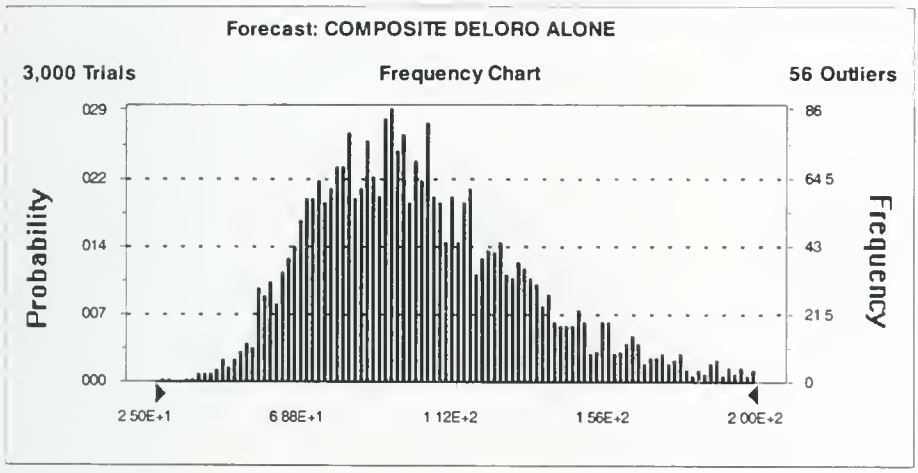
Percentiles:

Percentile	Value
0.0%	1.73E+02
2.5%	2.77E+02
5.0%	3.08E+02
50.0%	5.39E+02
95.0%	8.23E+02
97.5%	8.66E+02
100.0%	1.09E+03

End of Forecast

Forecast: COMPOSITE DELORO ALONE **Cell: C55**

Statistics:	Value
Trials	3000
Mean	1.04E+02
Median	9.84E+01
Mode	---
Standard Deviation	3.46E+01
Variance	1.20E+03
Skewness	1.26
Kurtosis	6.30
Coeff. of Variability	0.33
Range Minimum	2.83E+01
Range Maximum	3.64E+02
Range Width	3.36E+02
Mean Std. Error	6.32E-01



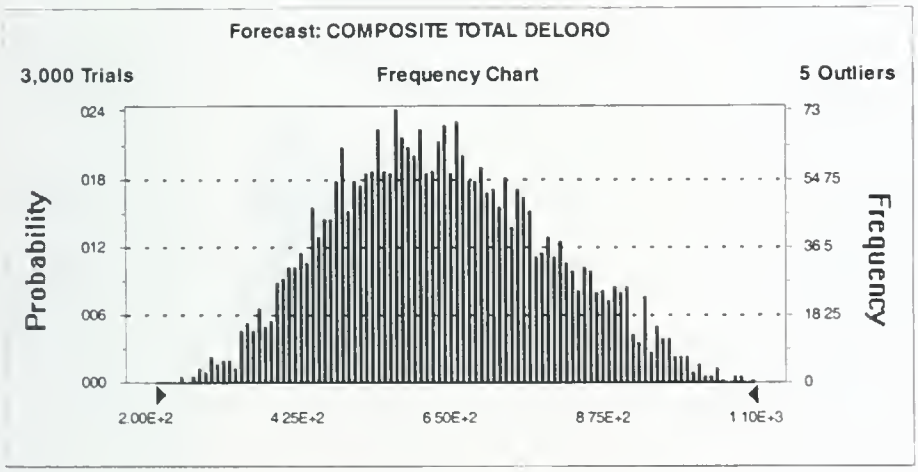
Percentiles:

Percentile	Value
0.0%	2.83E+01
2.5%	5.53E+01
5.0%	5.95E+01
50.0%	9.84E+01
95.0%	1.68E+02
97.5%	1.91E+02
100.0%	3.64E+02

End of Forecast

Forecast: COMPOSITE TOTAL DELORO **Cell: D55**

Statistics:	Value
Trials	3000
Mean	6.31E+02
Median	6.23E+02
Mode	---
Standard Deviation	1.60E+02
Variance	2.57E+04
Skewness	0.25
Kurtosis	2.60
Coeff. of Variability	0.25
Range Minimum	2.39E+02
Range Maximum	1.19E+03
Range Width	9.47E+02
Mean Std. Error	2.93E+00



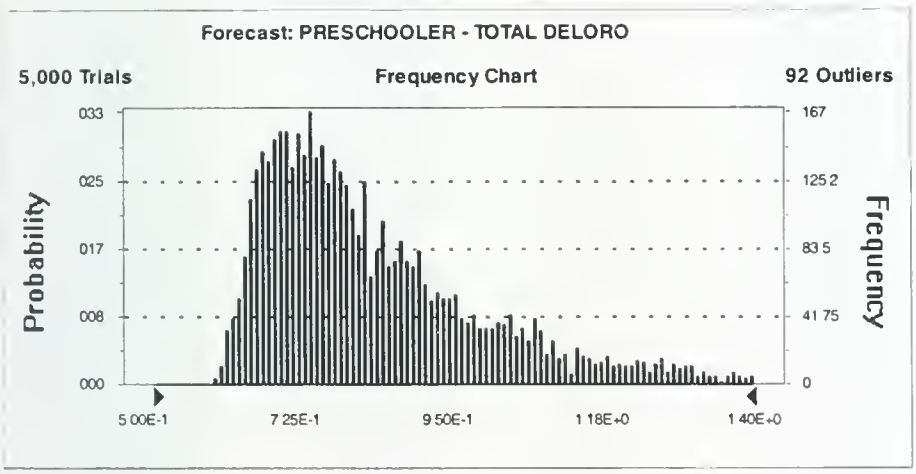
Percentiles:

Percentile	Value
0.0%	2.39E+02
2.5%	3.49E+02
5.0%	3.84E+02
50.0%	6.23E+02
95.0%	9.08E+02
97.5%	9.54E+02
100.0%	1.19E+03

End of Forecast

Forecast: PRESCHOOLER - TOTAL DELORO **Cell: D16**

Statistics:	Value
Trials	5000
Mean	8.44E-01
Median	7.89E-01
Mode	---
Standard Deviation	1.91E-01
Variance	3.66E-02
Skewness	1.82
Kurtosis	7.95
Coeff. of Variability	0.23
Range Minimum	5.92E-01
Range Maximum	2.29E+00
Range Width	1.70E+00
Mean Std. Error	2.70E-03



Percentiles:

Percentile	Value
0.0%	5.92E-01
2.5%	6.33E-01
5.0%	6.46E-01
50.0%	7.89E-01
95.0%	1.23E+00
97.5%	1.34E+00
100.0%	2.29E+00

End of Forecast

SUMMARY TABLE - ARSENIC CANCER RISK LEVELS (CRLs)

Home Garden Produce Consumption

Whole Town

ARSENIC	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	2 62E-05	8 27E-06	3 46E-06	9 97E-06	2 01E-05	1 41E-05	2 42E-06	6 66E-07	1 62E-06	5 22E-06	3 87E-05	6 36E-06	4 96E-06	1 19E-05	2 24E-05
PRESCHOOL CHILD	2 00E-04	2 99E-05	2 27E-05	6 81E-05	1 61E-04	1 05E-04	1 85E-05	8 02E-06	1 50E-05	3 80E-05	2 90E-04	4 84E-05	3 06E-04	3 86E-04	3 86E-04
CHILD	2 68E-04	2 42E-05	2 37E-05	9 32E-05	2 16E-04	1 14E-04	1 49E-05	6 36E-06	1 37E-05	2 97E-05	3 66E-04	3 66E-05	3 43E-05	1 05E-04	2 27E-04
ADOLESCENT	2 09E-04	3 03E-05	2 12E-05	7 23E-05	1 67E-04	9 20E-05	9 85E-06	4 48E-06	1 02E-05	2 24E-05	2 69E-04	3 84E-05	2 94E-05	8 15E-05	1 67E-04
ADULT	6 97E-04	1 65E-04	1 02E-04	2 62E-04	5 16E-04	5 19E-04	6 85E-05	2 97E-05	6 12E-05	1 25E-04	1 14E-03	2 23E-04	1 48E-04	3 14E-04	5 72E-04
COMPOSITE	1 42E-03	2 58E-04	3 19E-04	8 37E-04	6 17E-04	4 09E-04	1 14E-04	8 57E-05	1 09E-04	1 79E-04	1 71E-03	3 81E-04	4 02E-04	6 27E-04	8 12E-04

zone 1

ARSENIC	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	2 62E-05	8 27E-06	3 46E-06	1 01E-05	2 03E-05	4 59E-06	1 51E-06	4 51E-07	1 25E-06	3 59E-06	2 92E-05	7 44E-06	4 43E-06	1 13E-05	2 15E-05
PRESCHOOL CHILD	2 00E-04	2 98E-05	2 21E-05	6 90E-05	7 69E-05	3 74E-05	1 28E-05	3 84E-06	1 05E-05	2 81E-05	2 22E-04	3 98E-05	2 69E-05	7 88E-05	1 61E-04
CHILD	2 68E-04	2 42E-05	2 36E-05	9 15E-05	2 18E-04	3 68E-05	1 02E-05	4 50E-06	1 01E-05	2 30E-05	3 09E-04	3 18E-05	3 11E-05	1 00E-04	2 27E-04
ADOLESCENT	2 09E-04	3 03E-05	2 18E-05	7 13E-05	1 58E-04	3 07E-05	8 90E-06	4 50E-06	1 01E-05	2 30E-05	2 27E-04	3 55E-05	2 72E-05	7 81E-05	1 64E-04
ADULT	6 97E-04	1 65E-04	1 04E-04	2 63E-04	5 18E-04	2 02E-04	5 23E-05	2 93E-06	7 25E-06	1 68E-05	8 22E-04	2 06E-04	1 35E-04	3 02E-04	5 61E-04
COMPOSITE	1 42E-03	2 58E-04	3 18E-04	5 40E-04	8 19E-04	1 42E-04	6 97E-05	4 63E-05	8 15E-05	1 44E-04	1 44E-03	3 21E-04	3 74E-04	8 02E-04	8 88E-04

zone 2

ARSENIC	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	2 62E-05	8 27E-06	3 41E-06	1 01E-05	2 00E-05	5 61E-06	1 72E-06	5 12E-07	1 44E-06	3 83E-06	3 04E-05	7 86E-06	4 58E-06	1 14E-05	2 15E-05
PRESCHOOL CHILD	2 00E-04	2 99E-05	2 26E-05	6 94E-05	1 50E-04	4 59E-05	1 41E-05	4 74E-06	1 20E-05	3 02E-05	2 31E-04	4 10E-05	3 14E-05	7 99E-05	1 62E-04
CHILD	2 68E-04	2 42E-05	2 37E-05	9 15E-05	2 12E-04	4 66E-05	1 13E-05	5 03E-06	1 13E-05	2 60E-05	3 19E-04	3 30E-05	3 23E-05	1 01E-04	2 24E-04
ADOLESCENT	2 09E-04	3 03E-05	2 04E-05	7 18E-05	1 61E-04	3 84E-05	7 69E-06	5 03E-06	1 13E-05	2 60E-05	2 35E-04	3 62E-05	2 66E-05	7 83E-05	1 66E-04
ADULT	6 97E-04	1 65E-04	1 01E-04	2 71E-04	5 13E-04	2 42E-04	5 61E-05	3 48E-06	8 07E-06	1 89E-05	8 61E-04	2 10E-04	1 36E-04	3 13E-04	5 55E-04
COMPOSITE	1 42E-03	2 58E-04	3 16E-04	5 42E-04	8 16E-04	1 78E-04	8 08E-05	5 42E-05	8 85E-05	1 55E-04	1 47E-03	3 26E-04	3 77E-04	8 11E-04	8 90E-04

ZONE 3

ARSENIC	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	2 62E-05	8 27E-06	3 30E-06	9 79E-06	2 02E-05	1 39E-05	2 73E-06	8 41E-07	2 51E-06	7 23E-06	3 84E-05	6 67E-06	5 46E-06	1 27E-05	2 35E-05
PRESCHOOL CHILD	2 00E-04	2 99E-05	2 23E-05	6 89E-05	1 50E-04	1 02E-04	2 05E-05	7 23E-06	1 67E-05	4 66E-05	2 87E-04	4 74E-05	3 59E-05	8 73E-05	1 71E-04
CHILD	2 68E-04	2 42E-05	2 28E-05	9 36E-05	2 21E-04	1 11E-04	1 66E-05	7 47E-06	1 75E-05	3 93E-05	3 83E-04	3 62E-05	3 63E-05	1 10E-04	2 37E-04
ADOLESCENT	2 09E-04	3 03E-05	2 17E-05	7 20E-05	1 58E-04	8 93E-05	1 09E-05	7 47E-06	1 75E-05	3 93E-05	2 86E-04	3 95E-05	3 18E-05	8 36E-05	1 89E-04
ADULT	6 97E-04	1 65E-04	9 94E-05	2 65E-04	5 12E-04	5 04E-04	7 40E-05	5 65E-06	1 26E-05	2 76E-05	1 12E-03	2 28E-04	1 62E-04	3 33E-04	5 62E-04
COMPOSITE	1 42E-03	2 58E-04	3 17E-04	5 40E-04	8 09E-04	3 97E-04	1 25E-04	7 52E-05	1 34E-04	2 30E-04	1 69E-03	3 62E-04	4 26E-04	8 61E-04	8 40E-04

ZONE 4

ARSENIC	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	2 62E-05	8 27E-06	3 46E-06	9 98E-06	1 98E-05	1 73E-05	3 55E-06	9 29E-07	2 47E-06	6 69E-06	4 19E-05	9 49E-06	5 56E-06	1 26E-05	2 27E-05
PRESCHOOL CHILD	2 00E-04	2 99E-05	2 31E-05	6 83E-05	1 47E-04	1 26E-04	2 56E-05	7 60E-06	1 85E-05	4 20E-05	3 10E-04	5 25E-05	3 62E-05	8 44E-05	1 67E-04
CHILD	2 68E-04	2 42E-05	2 34E-05	9 33E-05	2 11E-04	1 36E-04	2 07E-05	7 80E-06	1 67E-05	3 48E-05	4 10E-04	4 24E-05	3 70E-05	1 08E-04	2 26E-04
ADOLESCENT	2 09E-04	3 03E-05	2 16E-05	7 05E-05	1 59E-04	1 11E-04	1 34E-05	7 60E-06	1 67E-05	3 48E-05	3 07E-04	4 20E-05	3 17E-05	8 21E-05	1 71E-04
ADULT	6 97E-04	1 65E-04	1 00E-04	2 58E-04	5 15E-04	6 14E-04	8 81E-05	5 99E-06	1 23E-05	2 55E-05	1 23E-03	2 42E-04	1 57E-04	3 25E-04	5 84E-04
COMPOSITE	1 42E-03	2 58E-04	3 15E-04	5 30E-04	8 16E-04	4 89E-04	1 61E-04	7 84E-05	1 30E-04	2 06E-04	1 79E-03	3 59E-04	4 14E-04	8 41E-04	8 32E-04

SUMMARY TABLE

CANCER RISK LEVELS (CRLs) DUE TO ARSENIC EXPOSURE VIA INHALATION ROUTE ONLY

Whole Town

ARSENIC	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	1 97E-07	1 85E-08	1 74E-08	6.34E-08	1 68E-07	6 04E-09	1 62E-09	1 02E-09	2 67E-09	7 37E-09	3 08E-08	3 94E-09	3 94E-09	1 10E-08	2 70E-08
PRESCHOOL CHILD	3 92E-06	3.67E-07	3.48E-07	1.28E-06	3.01E-06	1.20E-07	3.21E-06	2.13E-06	5.50E-06	1.34E-07	6.11E-07	7.61E-06	6.87E-07	6 67E-07	6 67E-07
CHILD	4 41E-06	4 44E-07	4 21E-07	1 55E-06	3 56E-06	1.35E-07	2 97E-08	2 42E-08	6 05E-08	1.39E-07	6 87E-07	1 76E-07	1 43E-07	4 25E-07	9 41E-07
ADOLESCENT	3.16E-06	3.06E-07	2.93E-07	1.05E-06	2.41E-06	9.69E-08	1.76E-06	1.57E-06	3.87E-06	6.69E-08	4.93E-07	1.45E-07	1.10E-07	3.25E-07	7.47E-07
ADULT	1 64E-05	1 61E-06	1 58E-06	5 52E-06	1 21E-05	5 01E-07	9 41E-08	8 42E-08	2 02E-07	4 54E-07	2 54E-06	7 67E-07	5 80E-07	1 67E-06	3 67E-06
COMPOSITE	2 81E-05	2.75E-06	2.94E-06	1.00E-05	1.89E-05	4.38E-07	1.75E-07	1.69E-07	3.76E-07	7.39E-07	3.94E-06	1.17E-06	1.04E-06	2.83E-06	5.28E-06

CANCER RISK LEVELS (CRLs) DUE TO ARSENIC EXPOSURE VIA ORAL/DERMAL ROUTES

Whole Town

ARSENIC	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	2 60E-05	6 26E-06	3 29E-06	9 75E-06	1 97E-05	1 41E-05	2 42E-06	6 64E-07	1 95E-06	5 26E-06	3 86E-05	8 35E-06	4 93E-06	1 17E-05	2 21E-05
PRESCHOOL CHILD	1.96E-04	2.95E-05	1.99E-05	6.86E-05	1.48E-04	1.05E-04	1.85E-05	6.17E-06	1.48E-05	3.72E-05	2.89E-04	4.53E-05	3.86E-04	3.86E-04	3.86E-04
CHILD	2 84E-04	2 38E-05	2 21E-05	9 10E-05	2 13E-04	1 14E-04	1 49E-05	6 40E-06	1 41E-05	3 00E-05	3 86E-04	3 64E-05	3 34E-05	1 05E-04	2 26E-04
ADOLESCENT	2.08E-04	3.00E-05	2.10E-05	7.08E-05	1.58E-04	9 19E-05	9 83E-06	4.53E-06	9.89E-06	2.22E-05	2.86E-04	3 83E-05	2.99E-05	6.10E-05	1.69E-04
ADULT	6 81E-04	1 64E-04	9 33E-05	2 52E-04	5 05E-04	5 18E-04	6 84E-05	2 89E-05	6 01E-05	1 26E-04	1 14E-03	2 22E-04	1 43E-04	3 09E-04	5 67E-04
COMPOSITE	1.39E-03	2.53E-04	3.04E-04	6.20E-04	8.02E-04	4.08E-04	1.14E-04	6.48E-05	1.07E-04	1.83E-04	1.70E-03	3.50E-04	3.92E-04	6.14E-04	9.10E-04

SUMMARY TABLE - ARSENIC CANCER RISK LEVELS (CRLs)

No Home Garden Produce Consumption

Whole Town

ARSENIC	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	2.62E-05	8.27E-06	3.46E-06	1.02E-05	2.00E-05	1.41E-05	2.42E-06	6.82E-07	1.93E-06	5.46E-06	3.87E-05	8.36E-06	5.11E-06	1.22E-05	2.23E-05
PRESCHOOL CHILD	1.99E-04	2.96E-05	2.29E-05	8.53E-05	1.52E-04	9.66E-05	1.76E-05	6.49E-06	1.40E-05	3.61E-05	2.83E-04	4.46E-05	3.79E-04	3.79E-04	3.79E-04
CHILD	2.87E-04	2.38E-05	2.39E-05	9.34E-05	2.17E-04	1.06E-04	1.39E-05	5.79E-06	1.24E-05	2.80E-05	3.79E-04	3.56E-05	3.34E-05	1.05E-04	2.29E-04
ADOLESCENT	2.06E-04	3.00E-05	2.20E-05	7.27E-05	1.58E-04	8.58E-05	8.84E-06	3.83E-06	8.99E-06	2.06E-05	2.82E-04	3.75E-05	2.90E-05	8.06E-05	1.66E-04
ADULT	8.93E-04	1.64E-04	9.66E-05	2.81E-04	5.18E-04	4.99E-04	8.42E-05	2.02E-05	5.55E-05	1.19E-04	1.11E-03	2.18E-04	1.38E-04	3.13E-04	5.73E-04
COMPOSITE	1.41E-03	2.53E-04	3.06E-04	8.39E-04	8.23E-04	3.83E-04	1.07E-04	6.86E-05	8.64E-05	1.68E-04	1.58E-03	3.44E-04	3.84E-04	8.23E-04	9.08E-04

zone 1

ARSENIC	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	2.62E-05	8.27E-06	3.38E-06	9.76E-06	2.00E-05	4.59E-06	1.51E-06	1.27E-04	1.28E-04	1.30E-04	2.92E-05	7.44E-06	4.41E-06	1.10E-05	2.13E-05
PRESCHOOL CHILD	1.99E-04	2.96E-05	2.16E-05	8.73E-05	1.49E-04	3.66E-05	1.25E-05	1.30E-03	1.30E-03	1.32E-03	2.21E-04	3.84E-05	2.85E-05	7.68E-05	1.59E-04
CHILD	2.87E-04	2.38E-05	2.34E-05	9.00E-05	2.13E-04	3.58E-05	9.93E-06	1.58E-03	1.59E-03	1.60E-03	3.08E-04	3.19E-05	3.06E-05	9.85E-05	2.23E-04
ADOLESCENT	2.06E-04	3.00E-05	2.13E-05	7.25E-05	1.67E-04	2.99E-05	8.58E-06	1.58E-03	1.59E-03	1.60E-03	2.26E-04	3.53E-05	2.69E-05	7.83E-05	1.62E-04
ADULT	8.93E-04	1.64E-04	1.01E-04	2.58E-04	5.10E-04	1.09E-04	5.13E-05	1.76E-03	1.76E-03	1.78E-03	8.18E-04	2.05E-04	1.34E-04	2.86E-04	5.55E-04
COMPOSITE	1.41E-03	2.53E-04	3.11E-04	8.32E-04	8.02E-04	1.39E-04	8.20E-05	4.76E-05	7.91E-05	1.43E-04	1.44E-03	3.19E-04	3.71E-04	8.05E-04	8.77E-04

zone 2

ARSENIC	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	2.62E-05	8.27E-06	3.31E-06	1.02E-05	1.99E-05	5.81E-06	1.72E-06	5.13E-07	1.44E-06	4.12E-06	3.04E-05	7.66E-06	4.40E-06	1.16E-05	2.14E-05
PRESCHOOL CHILD	1.99E-04	2.96E-05	2.24E-05	8.75E-05	1.46E-04	4.46E-05	1.37E-05	4.29E-06	1.12E-05	3.02E-05	2.29E-04	4.06E-05	3.06E-05	7.79E-05	1.57E-04
CHILD	2.87E-04	2.38E-05	2.34E-05	9.26E-05	2.19E-04	4.49E-05	1.09E-05	4.85E-06	1.07E-05	2.46E-05	3.17E-04	3.25E-05	3.19E-05	1.01E-04	2.28E-04
ADOLESCENT	2.06E-04	3.00E-05	2.07E-05	7.11E-05	1.58E-04	3.70E-05	7.21E-06	4.56E-06	1.07E-05	2.46E-05	2.34E-04	3.58E-05	2.69E-05	7.78E-05	1.64E-04
ADULT	8.93E-04	1.64E-04	1.01E-04	2.57E-04	5.19E-04	2.36E-04	5.43E-05	3.15E-06	7.40E-06	1.82E-05	8.55E-04	2.08E-04	1.35E-04	2.97E-04	5.57E-04
COMPOSITE	1.41E-03	2.53E-04	3.10E-04	8.34E-04	8.10E-04	1.70E-04	8.79E-05	5.08E-05	8.42E-05	1.81E-04	1.47E-03	3.25E-04	3.76E-04	8.04E-04	8.83E-04

ZONE 3

ARSENIC	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	2.62E-05	8.27E-06	3.37E-06	1.01E-05	2.01E-05	1.39E-05	2.73E-06	8.55E-07	2.49E-06	7.30E-06	3.84E-05	8.67E-06	5.37E-06	1.29E-05	2.35E-05
PRESCHOOL CHILD	1.99E-04	2.96E-05	2.19E-05	8.96E-05	1.52E-04	9.71E-05	1.94E-05	6.39E-06	1.70E-05	4.33E-05	2.82E-04	4.62E-05	3.46E-05	8.87E-05	1.69E-04
CHILD	2.87E-04	2.38E-05	2.23E-05	9.34E-05	2.13E-04	1.05E-04	1.52E-05	8.58E-06	1.50E-05	3.38E-05	3.77E-04	3.89E-05	3.43E-05	1.08E-04	2.28E-04
ADOLESCENT	2.06E-04	3.00E-05	2.13E-05	7.26E-05	1.59E-04	8.43E-05	8.71E-06	6.58E-06	1.60E-05	3.38E-05	2.81E-04	3.83E-05	3.06E-05	8.28E-05	1.69E-04
ADULT	8.93E-04	1.64E-04	1.02E-04	2.81E-04	5.09E-04	4.82E-04	8.86E-05	4.99E-06	1.07E-05	2.30E-05	1.10E-03	2.23E-04	1.51E-04	3.20E-04	5.72E-04
COMPOSITE	1.41E-03	2.53E-04	3.23E-04	8.33E-04	8.10E-04	3.77E-04	1.16E-04	6.82E-05	1.16E-04	1.99E-04	1.67E-03	3.53E-04	4.11E-04	8.36E-04	9.19E-04

ZONE 4

ARSENIC	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	2.62E-05	8.27E-06	3.33E-06	9.92E-06	2.02E-05	1.73E-05	3.55E-06	9.15E-07	2.52E-06	8.81E-06	4.19E-05	9.49E-06	5.34E-06	1.25E-05	2.35E-05
PRESCHOOL CHILD	1.99E-04	2.96E-05	2.27E-05	8.74E-05	1.51E-04	1.19E-04	2.39E-05	6.74E-06	1.64E-05	3.64E-05	3.04E-04	5.06E-05	3.44E-05	8.34E-05	1.58E-04
CHILD	2.87E-04	2.38E-05	2.31E-05	9.32E-05	2.16E-04	1.30E-04	1.88E-05	8.81E-06	1.51E-05	3.11E-05	4.02E-04	4.04E-05	3.49E-05	1.08E-04	2.29E-04
ADOLESCENT	2.06E-04	3.00E-05	2.16E-05	7.08E-05	1.57E-04	1.04E-04	1.17E-05	8.81E-06	1.51E-05	3.11E-05	3.01E-04	4.03E-05	3.01E-05	8.09E-05	1.58E-04
ADULT	8.93E-04	1.64E-04	1.02E-04	2.81E-04	5.06E-04	5.87E-04	9.02E-05	4.79E-06	1.06E-05	2.29E-05	1.21E-03	2.34E-04	1.53E-04	3.20E-04	5.67E-04
COMPOSITE	1.41E-03	2.53E-04	3.20E-04	8.32E-04	8.09E-04	4.65E-04	1.38E-04	7.29E-05	1.16E-04	1.88E-04	1.76E-03	3.75E-04	4.13E-04	8.31E-04	9.19E-04

SUMMARY OF NON-CARCINOGENIC ARSENIC RISK VALUES

Home Garden

Whole Town

ARSENIC	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	8.08E+00	1.95E+00	1.04E+00	3.08E+00	6.34E+00	4.38E+00	7.53E-01	2.09E-01	5.79E-01	1.65E+00	1.20E+01	2.60E+00	1.51E+00	3.74E+00	7.01E+00
PRESCHOOL CHILD	6.79E+00	1.02E+00	7.45E-01	2.35E+00	5.15E+00	3.63E+00	6.40E-01	2.03E-01	5.08E-01	1.29E+00	1.00E+01	1.57E+00	1.15E+00	2.87E+00	6.63E+00
CHILD	6.31E-06	5.28E-01	4.87E-01	2.00E+00	4.77E+00	2.54E+00	3.31E-01	1.36E-01	3.05E-01	1.36E-01	8.57E+00	8.10E-01	7.38E-01	2.31E+00	5.10E+00
ADOLESCENT	4.01E+00	6.83E-01	3.97E-01	1.40E+00	3.04E+00	1.79E+00	1.91E-01	8.38E-02	1.95E-01	8.38E-02	5.60E+00	7.45E-01	5.82E-01	1.58E+00	3.24E+00
ADULT	2.12E+00	5.09E-01	3.00E-01	7.97E-01	1.59E+00	1.61E+00	2.13E-01	8.95E-02	1.85E-01	8.95E-02	3.53E+00	6.90E-01	4.51E-01	9.77E-01	1.77E+00

ZONE 1

ARSENIC	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	8.08E+00	1.95E+00	1.04E+00	3.03E+00	6.17E+00	1.43E+00	4.69E-01	1.43E-01	3.93E-01	1.09E+00	9.07E+00	2.32E+00	1.34E+00	3.43E+00	6.64E+00
PRESCHOOL CHILD	6.79E+00	1.02E+00	7.64E-01	2.28E+00	5.11E+00	1.29E+00	4.40E-01	1.37E-01	3.69E-01	9.91E-01	7.66E+00	1.37E+00	1.02E+00	2.67E+00	6.53E+00
CHILD	6.31E+00	5.28E-01	4.94E-01	2.03E+00	4.74E+00	8.17E-01	2.26E-01	9.93E-02	2.25E-01	5.16E-01	6.85E+00	7.04E-01	6.78E-01	2.25E+00	4.94E+00
ADOLESCENT	4.01E+00	6.83E-01	4.05E-01	1.38E+00	3.03E+00	5.95E-01	1.34E-01	9.93E-02	2.25E-01	6.18E-01	4.41E+00	6.88E-01	5.16E-01	1.51E+00	3.19E+00
ADULT	2.12E+00	5.09E-01	3.05E-01	8.00E-01	1.56E+00	6.28E-01	1.63E-01	5.68E-02	1.40E-01	3.53E-01	2.55E+00	6.40E-01	4.16E-01	9.36E-01	1.71E+00

zone 2

ARSENIC	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	8.08E+00	1.95E+00	9.89E-01	3.13E+00	6.31E+00	1.80E+00	5.35E-01	1.60E-01	4.43E-01	1.24E+00	9.45E+00	2.38E+00	1.37E+00	3.60E+00	6.78E+00
PRESCHOOL CHILD	6.79E+00	1.02E+00	7.37E-01	2.35E+00	5.11E+00	1.58E+00	4.87E-01	1.52E-01	4.01E-01	1.04E+00	7.96E+00	1.41E+00	1.09E+00	2.75E+00	6.53E+00
CHILD	6.31E+00	5.28E-01	4.87E-01	2.01E+00	4.80E+00	1.03E+00	2.51E-01	1.12E-01	2.48E-01	5.77E-01	7.07E+00	7.29E-01	6.98E-01	2.25E+00	5.04E+00
ADOLESCENT	4.01E+00	6.83E-01	3.96E-01	1.41E+00	3.07E+00	7.45E-01	1.47E-01	1.12E-01	2.48E-01	5.77E-01	4.56E+00	7.01E-01	5.34E-01	1.55E+00	3.23E+00
ADULT	2.12E+00	5.09E-01	2.99E-01	7.94E-01	1.56E+00	7.51E-01	1.74E-01	6.58E-02	1.52E-01	3.76E-01	2.67E+00	6.52E-01	4.21E-01	9.51E-01	1.72E+00

zone 3

ARSENIC	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	8.08E+00	1.95E+00	1.04E+00	3.11E+00	6.27E+00	4.31E+00	8.49E-01	2.63E-01	7.93E-01	2.25E+00	1.20E+01	2.70E+00	1.72E+00	3.98E+00	7.37E+00
PRESCHOOL CHILD	6.79E+00	1.02E+00	7.45E-01	2.32E+00	6.06E+00	3.53E+00	7.07E-01	2.48E-01	6.69E-01	1.63E+00	9.90E+00	1.63E+00	1.26E+00	2.99E+00	6.65E+00
CHILD	6.31E+00	5.28E-01	4.95E-01	2.07E+00	4.77E+00	2.46E+00	3.67E-01	1.71E-01	3.88E-01	8.64E-01	8.50E+00	8.46E-01	8.28E-01	2.47E+00	5.20E+00
ADOLESCENT	4.01E+00	6.83E-01	4.10E-01	1.38E+00	3.09E+00	1.73E+00	2.11E-01	1.71E-01	3.88E-01	8.64E-01	5.55E+00	7.64E-01	6.07E-01	1.63E+00	3.33E+00
ADULT	2.12E+00	5.09E-01	2.93E-01	7.98E-01	1.57E+00	1.57E+00	2.30E-01	1.07E-01	2.42E-01	5.30E-01	3.49E+00	7.07E-01	4.79E-01	1.02E+00	1.81E+00

ZONE 4

ARSENIC	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	8.08E+00	1.95E+00	1.02E+00	2.99E+00	6.17E+00	5.38E+00	1.10E+00	2.93E-01	7.77E-01	2.02E+00	1.30E+01	2.95E+00	1.68E+00	3.87E+00	7.13E+00
PRESCHOOL CHILD	6.79E+00	1.02E+00	7.14E-01	2.28E+00	6.18E+00	4.34E+00	8.64E-01	2.68E-01	6.31E-01	1.47E+00	1.07E+01	1.81E+00	1.23E+00	2.95E+00	6.67E+00
CHILD	6.31E+00	5.28E-01	4.97E-01	2.05E+00	4.79E+00	3.06E+00	4.60E-01	1.77E-01	3.75E-01	7.80E-01	9.09E+00	9.39E-01	8.01E-01	2.43E+00	5.17E+00
ADOLESCENT	4.01E+00	6.83E-01	4.09E-01	1.40E+00	3.05E+00	2.15E+00	2.60E-01	1.77E-01	3.75E-01	7.80E-01	6.96E+00	8.14E-01	6.19E-01	1.64E+00	3.31E+00
ADULT	2.12E+00	5.09E-01	3.04E-01	7.92E-01	1.58E+00	1.91E+00	2.74E-01	1.19E-01	2.39E-01	4.98E-01	3.83E+00	7.51E-01	4.92E-01	1.01E+00	1.82E+00

SUMMARY OF NON-CARCINOGENIC ARSENIC RISK VALUES

No Home Garden

Whole Town

ARSENIC	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	8 08E+00	1 95E+00	1 04E+00	3 06E+00	6 24E+00	4 38E+00	7 53E-01	2 17E-01	5 98E-01	1 57E+00	1 20E+01	2 60E+00	1 53E+00	3 72E+00	6 95E+00
PRESCHOOL CHILD	6.76E+00	1.01E+00	7.35E-01	2.31E+00	5.07E+00	5.40E+00	6.08E-01	1.60E-01	4.80E-01	1.24E+00	9.77E+00	1.54E+00	1.11E+00	2.81E+00	5.58E+00
CHILD	6 28E-06	5 20E-01	5 07E-01	2 04E+00	4 77E+00	2 36E+00	3 08E-01	1 25E-01	2 78E-01	1 25E-01	8 40E+00	7 86E-01	7 22E-01	2 32E+00	5 08E+00
ADOLESCENT	3.99E+00	5.77E-01	3.89E-01	1.36E+00	3.00E+00	1.66E+00	1.74E-01	7.62E-02	1.75E-01	7.62E-02	5.48E+00	7.27E-01	6.65E-01	1.53E+00	3.21E+00
ADULT	2 11E+00	5 05E-01	2 89E-01	7 90E-01	1 60E+00	1 52E+00	2 00E-01	7 99E-02	1 71E-01	7 99E-02	3 44E+00	6 77E-01	4 33E-01	9 56E-01	1 77E+00

ZONE 1

ARSENIC	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	8 08E+00	1 95E+00	1 05E+00	2 99E+00	6 15E+00	1 43E+00	4 69E-01	1 37E-01	3 89E-01	1 08E+00	9 07E+00	2 32E+00	1 38E+00	3 39E+00	6 56E+00
PRESCHOOL CHILD	6.76E+00	1.01E+00	7.26E-01	2.29E+00	5.07E+00	1.26E+00	4.33E-01	1.28E-01	3.80E-01	1.02E+00	7.63E+00	1.36E+00	1.00E+00	2.57E+00	5.47E+00
CHILD	6 28E+00	5 20E-01	4 83E-01	1 97E+00	4 80E+00	7 95E-01	2 20E-01	9 42E-02	2 25E-01	5 10E-01	6 83E+00	6 99E-01	6 60E-01	2 21E+00	5 02E+00
ADOLESCENT	3.99E+00	5.77E-01	3.79E-01	1.33E+00	3.02E+00	5.79E-01	1.30E-01	9.42E-02	2.25E-01	5.10E-01	4.39E+00	6.83E-01	5.05E-01	1.48E+00	3.15E+00
ADULT	2 11E+00	5 05E-01	2 80E-01	7 87E-01	1 57E+00	6 17E-01	1 59E-01	5 28E-02	1 34E-01	3 51E-01	2 54E+00	6 37E-01	3 93E-01	9 20E-01	1 71E+00

zone 2

						Deterministic			Stochastic		Deterministic			Stochastic	
ARSENIC	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	8 08E+00	1 95E+00	1 05E+00	3 12E+00	6 34E+00	1 80E+00	5 35E-01	1 62E-01	4 49E-01	1 28E+00	9 45E+00	2 38E+00	1 41E+00	3 60E+00	6 84E+00
PRESCHOOL CHILD	6.76E+00	1.01E+00	7.14E-01	2.31E+00	5.07E+00	1.54E+00	4.74E-01	1.48E-01	3.82E-01	1.04E+00	7.91E+00	1.40E+00	1.00E+00	2.73E+00	5.55E+00
CHILD	6 28E+00	5 20E-01	4 70E-01	2 05E+00	4 71E+00	9 95E-01	2 41E-01	1 05E-01	2 39E-01	5 42E-01	7 03E+00	7 19E-01	6 90E-01	2 26E+00	4 98E+00
ADOLESCENT	3.99E+00	5.77E-01	4.01E-01	1.38E+00	3.05E+00	7.18E-01	1.40E-01	1.05E-01	2.39E-01	5.42E-01	4.53E+00	6.94E-01	5.26E-01	1.52E+00	3.22E+00
ADULT	2 11E+00	5 05E-01	2 96E-01	7 88E-01	1 57E+00	7 32E-01	1 69E-01	5 78E-02	1 44E-01	3 64E-01	2 65E+00	6 46E-01	4 15E-01	9 27E-01	1 73E+00

zone 3

						Deterministic			Stochastic		Deterministic			Stochastic	
ARSENIC	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	8 08E+00	1 95E+00	9 89E-01	3 05E+00	6 18E+00	4 31E+00	8 49E-01	2 60E-01	7 69E-01	2 21E+00	1 20E+01	2 70E+00	1 67E+00	3 94E+00	7 19E+00
PRESCHOOL CHILD	6.76E+00	1.01E+00	7.51E-01	2.35E+00	5.18E+00	3.35E+00	6.68E-01	2.33E-01	5.93E-01	1.50E+00	9.72E+00	1.60E+00	1.23E+00	2.97E+00	6.88E+00
CHILD	6 28E+00	5 20E-01	4 78E-01	2 03E+00	4 68E+00	2 33E+00	3 38E-01	1 47E-01	3 33E-01	7 69E-01	8 36E+00	8 16E-01	7 83E-01	2 37E+00	5 07E+00
ADOLESCENT	3.99E+00	5.77E-01	4.01E-01	1.34E+00	3.11E+00	1.64E+00	1.88E-01	1.47E-01	3.33E-01	7.69E-01	5.45E+00	7.42E-01	5.91E-01	1.66E+00	3.32E+00
ADULT	2 11E+00	5 05E-01	3 06E-01	8 06E-01	1 60E+00	1 50E+00	2 13E-01	9 36E-02	2 07E-01	4 57E-01	3 42E+00	6 91E-01	4 79E-01	1 00E+00	1 81E+00

ZONE 4

ARSENIC	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	8 08E+00	1 95E+00	1 04E+00	3 02E+00	6 21E+00	5 38E+00	1 10E+00	2 81E-01	7 48E-01	2 01E+00	1 30E+01	2 95E+00	1 63E+00	3 83E+00	7 14E+00
PRESCHOOL CHILD	6.76E+00	1.01E+00	7.48E-01	2.40E+00	5.02E+00	4.13E+00	5.25E-01	2.30E-01	5.80E-01	1.41E+00	1.05E+01	1.78E+00	1.22E+00	3.00E+00	5.70E+00
CHILD	6 28E+00	5 20E-01	4 74E-01	2 03E+00	4 93E+00	2 89E+00	4 17E-01	1 49E-01	3 24E-01	6 80E-01	8 93E+00	8 95E-01	7 53E-01	2 34E+00	5 24E+00
ADOLESCENT	3.99E+00	5.77E-01	4.06E-01	1.35E+00	3.06E+00	2.03E+00	2.28E-01	1.49E-01	3.24E-01	6.80E-01	5.84E+00	7.82E-01	5.55E-01	1.56E+00	3.27E+00
ADULT	2 11E+00	5 05E-01	2 94E-01	7 90E-01	1 56E+00	1 82E+00	2 49E-01	9 77E-02	2 05E-01	4 50E-01	3 75E+00	7 27E-01	4 56E-01	9 83E-01	1 77E+00

SUMMARY TABLE OF EXPOSURE RATIO (ER) VALUES FOR COBALT

Home Garden

Whole Town

COBALT	TYPICAL ONTARIO BKG. 100% BACKGROUND		DELORO ALONE (Incremental)		DELORO INCLUDING BACKGROUND (Site plus Bkg.)	
RECEPTOR	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean
INFANT	1.82E+00	9.45E-01	3.61E-02	9.29E-03	5.26E-01	3.09E-01
PRESCHOOL CHILD	3.51E+00	1.20E+00	3.99E-02	1.10E-02	6.08E-01	2.52E-01
CHILD	2.50E+00	9.07E-01	2.50E-02	6.16E-03	4.03E-01	3.40E-01
ADOLESCENT	1.56E+00	5.44E-01	1.39E-02	3.12E-03	2.45E-01	2.46E-01
ADULT	1.30E+00	4.59E-01	1.19E-02	2.72E-03	2.04E-01	2.08E-01

ZONE 1

COBALT	TYPICAL ONTARIO BKG. 100% BACKGROUND		DELORO ALONE (Incremental)		DELORO INCLUDING BACKGROUND (Site plus Bkg.)	
RECEPTOR	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean
INFANT	1.82E+00	9.45E-01	1.61E-02	6.86E-03	5.06E-01	3.07E-01
PRESCHOOL CHILD	3.51E+00	1.20E+00	2.19E-02	9.04E-03	5.90E-01	2.50E-01
CHILD	2.50E+00	9.07E-01	1.44E-02	5.22E-03	3.92E-01	3.39E-01
ADOLESCENT	1.56E+00	5.44E-01	8.90E-03	2.73E-03	2.40E-01	2.46E-01
ADULT	1.30E+00	4.59E-01	8.05E-03	2.43E-03	2.00E-01	4.25E-01

ZONE 2

COBALT	TYPICAL ONTARIO BKG. 100% BACKGROUND		DELORO ALONE (Incremental)		DELORO INCLUDING BACKGROUND (Site plus Bkg.)	
RECEPTOR	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean
INFANT	1.82E+00	9.45E-01	2.12E-02	7.49E-03	5.11E-01	3.07E-01
PRESCHOOL CHILD	3.51E+00	1.20E+00	2.68E-02	9.53E-03	5.95E-01	2.50E-01
CHILD	2.50E+00	9.07E-01	1.74E-02	5.45E-03	3.95E-01	3.39E-01
ADOLESCENT	1.56E+00	5.44E-01	1.03E-02	2.83E-03	2.42E-01	2.46E-01
ADULT	1.30E+00	4.59E-01	9.18E-03	2.50E-03	2.01E-01	4.25E-01

ZONE 3

COBALT	TYPICAL ONTARIO BKG. 100% BACKGROUND		DELORO ALONE (Incremental)		DELORO INCLUDING BACKGROUND (Site plus Bkg.)	
RECEPTOR	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean
INFANT	1.82E+00	9.45E-01	3.54E-02	1.04E-02	5.25E-01	3.10E-01
PRESCHOOL CHILD	3.51E+00	1.20E+00	3.83E-02	1.20E-02	6.07E-01	2.53E-01
CHILD	2.50E+00	9.07E-01	2.39E-02	6.70E-03	4.02E-01	3.41E-01
ADOLESCENT	1.56E+00	5.44E-01	1.32E-02	3.37E-03	2.45E-01	2.47E-01
ADULT	1.30E+00	4.59E-01	1.13E-02	2.92E-03	2.04E-01	4.25E-01

ZONE 4

COBALT	TYPICAL ONTARIO BKG. 100% BACKGROUND		DELORO ALONE (Incremental)		DELORO INCLUDING BACKGROUND (Site plus Bkg.)	
RECEPTOR	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean
INFANT	1.82E+00	9.45E-01	4.95E-02	1.19E-02	5.39E-01	3.12E-01
PRESCHOOL CHILD	3.51E+00	1.20E+00	5.06E-02	1.31E-02	6.19E-01	2.54E-01
CHILD	2.50E+00	9.07E-01	3.10E-02	7.16E-03	4.09E-01	3.41E-01
ADOLESCENT	1.56E+00	5.44E-01	1.65E-02	3.52E-03	2.48E-01	2.47E-01
ADULT	1.30E+00	4.59E-01	1.39E-02	3.02E-03	2.06E-01	4.26E-01

SUMMARY OF HUMAN HEALTH EXPOSURE RATIOS FOR LEAD

Home Garden

Whole Town

LEAD	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th %	95th %	Plausible max	mean	5th %	50th %	95th %	Plausible max	mean	5th %	50th%	95th %
INFANT	2 48E+00	9 86E-01	8 37E-01	1 06E+00	1 72E+00	2.15E+00	2.78E-01	5 70E-02	2 65E-01	1 01E+00	3 11E+00	1 05E+00	8 30E-01	1 08E+00	1 90E+00
PRESCHOOL CHILD	2.55E+00	9.13E-01	7.61E-01	9.93E-01	1.59E+00	4.29E+00	5.70E-01	1.81E-01	6.28E-01	1.95E+00	5.07E+00	1.17E+00	7.98E-01	1.25E+00	2.59E+00
CHILD	1 57E+00	5 97E-01	5 09E-01	6 61E-01	1 03E+00	2 86E+00	3 54E-01	1 17E-01	3 90E-01	1 28E+00	3 35E+00	7 74E-01	5 45E-01	8 43E-01	1 75E+00
ADOLESCENT	1.06E+00	3.71E-01	3.27E-01	4.25E-01	6.82E-01	1.75E+00	2.19E-01	7.27E-02	2.55E-01	8.11E-01	2.07E+00	4.88E-01	3.57E-01	5.67E-01	1.12E+00
ADULT	1 19E+00	4 25E-01	3 87E-01	4 91E-01	7 88E-01	1 35E+00	1 65E-01	6 38E-02	2 10E-01	6 08E-01	1 75E+00	4 99E-01	4 10E-01	5 79E-01	9 86E-01

ZONE 1

LEAD	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	2 48E+00	9 86E-01	8 39E-01	1 05E+00	1 70E+00	1 32E+00	1 08E-01	3 05E-02	1 32E-01	4 95E-01	2 28E+00	8 84E-01	8 04E-01	9 44E-01	1 40E+00
PRESCHOOL CHILD	2.55E+00	9.13E-01	7.59E-01	9.95E-01	1.65E+00	3.42E+00	2.13E-01	8.02E-02	2.78E-01	8.26E-01	4.19E+00	8.14E-01	6.92E-01	9.09E-01	1.49E+00
CHILD	1 57E+00	5 97E-01	3 28E-01	6 62E-01	1 07E+00	8 02E+01	1 63E+01	5 12E-02	1 74E-01	5 45E-01	2 94E+00	5 51E-01	4 76E-01	6 26E-01	1 04E+00
ADOLESCENT	1.06E+00	3.71E-01	5.05E-01	4.24E-01	6.93E-01	3.26E-03	6.13E-02	3.39E-02	1.16E-01	3.58E-01	1.91E+00	3.51E-01	3.15E-01	4.16E-01	6.85E-01
ADULT	1 19E+00	4 25E-01	3 88E-01	4 89E-01	7 71E-01	3 15E-03	6 24E-02	2 89E-02	9 30E-02	2 71E-01	1 84E+00	3 99E-01	3 69E-01	4 59E-01	6 68E-01

zone 2

LEAD	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	2 48E+00	9 86E-01	8 39E-01	1 05E+00	1 70E+00	9 85E-01	1 26E-01	5 05E-02	2 50E-01	1 14E+00	1 95E+00	9 03E-01	8 27E-01	1 07E+00	2 02E+00
PRESCHOOL CHILD	2.55E+00	9.13E-01	7.59E-01	9.95E-01	1.65E+00	1.80E+00	2.51E-01	1.40E-01	6.43E-01	2.21E+00	2.57E+00	8.52E-01	7.52E-01	1.27E+00	2.87E+00
CHILD	1 57E+00	5 97E-01	3 28E-01	6 62E-01	1 07E+00	1 18E+00	1 56E-01	8 61E-02	3 88E-01	1 49E+00	1 68E+00	5 75E-01	5 19E-01	8 43E-01	1 95E+00
ADOLESCENT	1.06E+00	3.71E-01	5.05E-01	4.24E-01	6.93E-01	7.37E-01	9.59E-02	5.74E-02	2.66E-01	9.29E-01	1.06E+00	3.85E-01	3.42E-01	5.68E-01	1.24E+00
ADULT	1 19E+00	4 25E-01	3 88E-01	4 89E-01	7 71E-01	6 00E-01	7 33E-02	4 76E-02	2 13E-01	6 97E-01	1 00E+00	4 10E-01	3 95E-01	5 80E-01	1 07E+00

zone 3

LEAD	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	2 48E+00	9 86E-01	8 39E-01	1 05E+00	1 70E+00	2 52E+00	3 61E-01	9 08E-02	4 14E-01	1 76E+00	3 48E+00	1 14E+00	8 66E-01	1 23E+00	2 67E+00
PRESCHOOL CHILD	2.55E+00	9.13E-01	7.59E-01	9.95E-01	1.65E+00	5.08E+00	7.42E-01	3.65E-01	1.10E+00	3.45E+00	5.86E+00	1.34E+00	9.74E-01	1.73E+00	4.10E+00
CHILD	1 57E+00	5 97E-01	3 28E-01	6 62E-01	1 07E+00	3 39E+00	4 62E-01	2 27E-01	7 01E-01	2 30E+00	3 88E+00	8 81E-01	6 52E-01	1 16E+00	2 80E+00
ADOLESCENT	1.06E+00	3.71E-01	5.05E-01	4.24E-01	6.93E-01	2.07E+00	2.65E-01	1.53E-01	4.73E-01	1.42E+00	2.39E+00	6.54E-01	4.40E-01	7.73E-01	1.72E+00
ADULT	1 19E+00	4 25E-01	3 88E-01	4 89E-01	7 71E-01	1 59E+00	2 14E-01	1 19E-01	3 65E-01	1 09E+00	1 99E+00	5 50E-01	4 70E-01	7 34E-01	1 47E+00

ZONE 4

LEAD	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	2 48E+00	9 86E-01	8 39E-01	1 05E+00	1 70E+00	1 30E+00	2 23E-01	5 18E-02	2 15E-01	7 57E-01	2 27E+00	9 99E-01	8 23E-01	1 03E+00	1 67E+00
PRESCHOOL CHILD	2.55E+00	9.13E-01	7.59E-01	9.95E-01	1.65E+00	2.48E+00	4.54E-01	1.96E-01	4.98E-01	1.27E+00	3.26E+00	1.05E+00	8.08E-01	1.13E+00	1.93E+00
CHILD	1 57E+00	5 97E-01	3 28E-01	6 62E-01	1 07E+00	1 64E+00	2 82E-01	1 23E-01	3 17E-01	8 85E-01	2 14E+00	7 01E-01	5 47E-01	7 73E-01	1 35E+00
ADOLESCENT	1.06E+00	3.71E-01	5.05E-01	4.24E-01	6.93E-01	1.01E+00	1.74E-01	9.24E-02	2.10E-01	6.44E-01	1.34E+00	4.43E-01	3.65E-01	5.11E-01	8.81E-01
ADULT	1 19E+00	4 25E-01	3 88E-01	4 89E-01	7 71E-01	8 05E-01	1 31E-01	7 12E-02	1 66E-01	4 12E-01	1 21E+00	4 68E-01	4 15E-01	5 30E-01	8 06E-01

SUMMARY OF HUMAN HEALTH EXPOSURE RATIOS FOR LEAD

No Home Garden

Whole Town

LEAD	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	2.47E+00	9.85E-01	8.42E-01	1.05E+00	1.71E+00	2.15E+00	2.78E-01	5.91E-02	2.58E-01	1.08E+00	3.11E+00	1.05E+00	8.34E-01	1.07E+00	1.98E+00
PRESCHOOL CHILD	2.14E+00	7.53E-01	6.58E-01	8.29E-01	1.39E+00	1.21E+00	1.48E-01	4.28E-02	1.60E-01	5.45E-01	1.99E+00	7.46E-01	6.46E-01	7.89E-01	1.23E+00
CHILD	1.28E+00	4.90E-01	4.42E-01	5.55E-01	8.84E-01	6.35E-01	5.80E-02	2.23E-02	7.98E-02	2.38E-01	1.13E+00	4.77E-01	4.36E-01	5.30E-01	7.63E-01
ADOLESCENT	6.79E-01	3.01E-01	2.82E-01	3.52E-01	5.89E-01	2.58E-01	1.12E-02	1.67E-02	4.91E-02	1.15E-01	6.84E-01	2.80E-01	2.90E-01	3.46E-01	4.61E-01
ADULT	1.05E+00	3.71E-01	3.48E-01	4.36E-01	7.23E-01	2.59E-01	1.11E-02	1.52E-02	4.54E-02	1.05E-01	6.59E-01	3.45E-01	3.50E-01	4.05E-01	5.24E-01

ZONE 1

LEAD	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	2.47E+00	9.85E-01	8.42E-01	1.05E+00	1.71E+00	1.32E+00	1.08E-01	3.20E-02	1.37E-01	4.78E-01	2.28E+00	8.84E-01	8.06E-01	9.55E-01	1.40E+00
PRESCHOOL CHILD	2.14E+00	7.53E-01	6.58E-01	8.29E-01	1.39E+00	2.35E+00	6.05E-02	2.37E-02	9.49E-02	3.04E-01	3.13E+00	6.61E-01	6.25E-01	7.24E-01	9.89E-01
CHILD	1.28E+00	4.90E-01	4.42E-01	5.55E-01	8.84E-01	8.02E+01	1.63E+01	1.24E-02	5.13E-02	1.42E-01	2.15E+00	4.44E-01	4.27E-01	4.99E-01	6.64E-01
ADOLESCENT	6.79E-01	3.01E-01	2.82E-01	3.52E-01	5.89E-01	3.26E-03	6.46E-03	6.60E-03	3.07E-02	8.52E-02	1.38E+00	2.76E-01	2.81E-01	3.27E-01	4.35E-01
ADULT	1.05E+00	3.71E-01	3.48E-01	4.36E-01	7.23E-01	3.15E-03	7.06E-03	8.25E-03	2.92E-02	7.77E-02	1.38E+00	3.43E-01	3.42E-01	3.90E-01	4.92E-01

zone 2

						Deterministic		Stochastic			Deterministic			Stochastic	
LEAD	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	2.47E+00	9.85E-01	8.42E-01	1.05E+00	1.71E+00	9.85E-01	1.26E-01	4.81E-02	2.45E-01	1.09E+00	1.95E+00	9.03E-01	8.25E-01	1.06E+00	1.99E+00
PRESCHOOL CHILD	2.14E+00	7.53E-01	6.58E-01	8.29E-01	1.39E+00	1.80E+00	2.61E-01	3.23E-02	1.52E-01	6.72E-01	1.40E+00	6.70E-01	6.34E-01	7.81E-01	1.24E+00
CHILD	1.28E+00	4.90E-01	4.42E-01	5.55E-01	8.84E-01	1.18E+00	1.56E-01	1.85E-02	7.74E-02	2.63E-01	8.35E-01	4.48E-01	4.33E-01	5.26E-01	7.76E-01
ADOLESCENT	6.79E-01	3.01E-01	2.82E-01	3.52E-01	5.89E-01	7.37E-01	9.59E-02	1.34E-02	4.73E-02	1.24E-01	4.97E-01	2.76E-01	2.87E-01	3.44E-01	4.61E-01
ADULT	1.05E+00	3.71E-01	3.48E-01	4.36E-01	7.23E-01	6.00E-01	7.33E-02	1.22E-02	4.34E-02	1.12E-01	5.86E-01	3.44E-01	3.48E-01	4.03E-01	5.22E-01

zone 3

						Deterministic		Stochastic			Deterministic			Stochastic	
LEAD	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	2.47E+00	9.85E-01	8.37E-01	1.05E+00	1.70E+00	2.52E+00	3.61E-01	9.36E-02	4.03E-01	1.60E+00	3.48E+00	1.14E+00	8.68E-01	1.21E+00	2.48E+00
PRESCHOOL CHILD	2.14E+00	7.53E-01	6.58E-01	8.30E-01	1.39E+00	1.40E+00	1.67E-01	5.79E-02	2.27E-01	8.45E-01	2.17E+00	7.67E-01	6.67E-01	8.67E-01	1.52E+00
CHILD	1.28E+00	4.90E-01	4.41E-01	5.55E-01	8.80E-01	7.28E-01	7.40E-02	3.03E-02	1.12E-01	3.75E-01	1.22E+00	4.93E-01	4.45E-01	5.59E-01	8.89E-01
ADOLESCENT	6.79E-01	3.01E-01	2.83E-01	3.51E-01	5.82E-01	2.65E-01	1.35E-02	2.44E-02	6.73E-02	1.61E-01	6.11E-01	2.83E-01	2.96E-01	3.66E-01	6.01E-01
ADULT	1.05E+00	3.71E-01	3.48E-01	4.35E-01	6.92E-01	2.82E-01	1.31E-02	2.32E-02	6.24E-02	1.40E-01	6.82E-01	3.49E-01	3.59E-01	4.23E-01	5.49E-01

ZONE 4

LEAD	TYPICAL ONTARIO BKG (100% bkg)					DELORO ALONE (incremental)					DELORO INCLUDING BKG (site + Bkg)				
RECEPTOR	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50th%	95th %	Plausible max	mean	5th %	50%th	95th %
INFANT	2.47E+00	9.85E-01	8.42E-01	1.06E+00	1.69E+00	1.30E+00	2.23E-01	5.90E-02	2.15E-01	7.18E-01	2.27E+00	9.99E-01	8.32E-01	1.03E+00	1.63E+00
PRESCHOOL CHILD	2.14E+00	7.53E-01	6.61E-01	8.30E-01	1.42E+00	7.67E-01	1.18E-01	3.71E-02	1.35E-01	4.19E-01	1.66E+00	7.18E-01	6.37E-01	7.81E-01	1.10E+00
CHILD	1.28E+00	4.90E-01	4.40E-01	5.51E-01	8.87E-01	4.19E-01	4.72E-02	1.93E-02	6.89E-02	1.89E-01	9.16E-01	4.66E-01	4.31E-01	5.15E-01	7.18E-01
ADOLESCENT	6.79E-01	3.01E-01	2.85E-01	3.52E-01	5.91E-01	1.95E-01	9.62E-03	1.54E-02	4.07E-02	9.96E-02	5.21E-01	2.79E-01	2.86E-01	3.36E-01	4.52E-01
ADULT	1.05E+00	3.71E-01	3.50E-01	4.34E-01	7.02E-01	2.06E-01	9.77E-03	1.32E-02	3.81E-02	9.08E-02	6.06E-01	3.46E-01	3.47E-01	3.98E-01	5.10E-01

SUMMARY TABLE OF EXPOSURE RATIO (ER) VALUES FOR SILVER

Home Garden Consumption

Whole Town

SILVER	TYPICAL ONTARIO BKG. 100% BACKGROUND		DELORO ALONE (Incremental)		DELORO INCLUDING BACKGROUND (Site plus Bkg.)	
RECEPTOR	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean
INFANT	1.97E+00	1.23E+00	6.50E-02	1.11E-02	2.02E+00	1.23E+00
PRESCHOOL CHILD	1.02E+00	6.24E-01	2.91E-01	4.40E-02	1.27E+00	6.52E-01
CHILD	5.24E-01	3.18E-01	2.05E-01	2.86E-02	6.96E-01	3.36E-01
ADOLESCENT	2.92E-01	1.76E-01	1.36E-01	1.89E-02	4.07E-01	1.89E-01
ADULT	2.46E-01	1.49E-01	1.05E-01	1.50E-02	3.33E-01	1.60E-01

ZONE 1

SILVER	TYPICAL ONTARIO BKG. 100% BACKGROUND		DELORO ALONE (Incremental)		DELORO INCLUDING BACKGROUND (Site plus Bkg.)	
RECEPTOR	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean
INFANT	1.97E+00	1.23E+00	1.35E-02	2.06E-03	1.97E+00	1.22E+00
PRESCHOOL CHILD	1.02E+00	6.24E-01	5.52E-02	7.26E-03	1.03E+00	6.15E-01
CHILD	5.24E-01	3.18E-01	3.88E-02	4.68E-03	5.29E-01	3.12E-01
ADOLESCENT	2.92E-01	1.76E-01	2.58E-02	3.08E-03	2.96E-01	1.74E-01
ADULT	2.46E-01	1.49E-01	2.01E-02	2.49E-03	2.48E-01	1.50E-01

ZONE 2

SILVER	TYPICAL ONTARIO BKG. 100% BACKGROUND		DELORO ALONE (Incremental)		DELORO INCLUDING BACKGROUND (Site plus Bkg.)	
RECEPTOR	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean
INFANT	1.97E+00	1.23E+00	3.33E-02	4.69E-03	1.99E+00	1.23E+00
PRESCHOOL CHILD	1.02E+00	6.24E-01	1.46E-01	1.79E-02	1.12E+00	6.26E-01
CHILD	5.24E-01	3.18E-01	1.03E-01	1.16E-02	5.93E-01	3.19E-01
ADOLESCENT	2.92E-01	1.76E-01	6.82E-02	7.69E-03	3.39E-01	1.78E-01
ADULT	2.46E-01	1.49E-01	5.26E-02	6.14E-03	2.81E-01	1.53E-01

ZONE 3

SILVER	TYPICAL ONTARIO BKG. 100% BACKGROUND		DELORO ALONE (Incremental)		DELORO INCLUDING BACKGROUND (Site plus Bkg.)	
RECEPTOR	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean
INFANT	1.97E+00	1.23E+00	6.60E-02	1.40E-02	2.02E+00	1.24E+00
PRESCHOOL CHILD	1.02E+00	6.24E-01	2.96E-01	5.59E-02	1.27E+00	6.64E-01
CHILD	5.24E-01	3.18E-01	2.09E-01	3.64E-02	6.99E-01	3.44E-01
ADOLESCENT	2.92E-01	1.76E-01	1.38E-01	2.41E-02	4.09E-01	1.95E-01
ADULT	2.46E-01	1.49E-01	1.06E-01	1.91E-02	3.34E-01	1.66E-01

ZONE 4

SILVER	TYPICAL ONTARIO BKG. 100% BACKGROUND		DELORO ALONE (Incremental)		DELORO INCLUDING BACKGROUND (Site plus Bkg.)	
RECEPTOR	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean
INFANT	1.97E+00	1.23E+00	6.60E-02	1.40E-02	2.02E+00	1.24E+00
PRESCHOOL CHILD	1.02E+00	6.24E-01	2.96E-01	5.59E-02	1.27E+00	6.64E-01
CHILD	5.24E-01	3.18E-01	2.09E-01	3.64E-02	6.99E-01	3.44E-01
ADOLESCENT	2.92E-01	1.76E-01	1.38E-01	2.41E-02	4.09E-01	1.95E-01
ADULT	2.46E-01	1.49E-01	1.06E-01	1.91E-02	3.34E-01	1.66E-01

SUMMARY TABLE OF EXPOSURE RATIO (ER) VALUES FOR SILVER

No Home Garden Consumption

Whole Town

SILVER	TYPICAL ONTARIO BKG. 100% BACKGROUND		DELORO ALONE (Incremental)		DELORO INCLUDING BACKGROUND (Site plus Bkg.)	
RECEPTOR	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean
INFANT	1.97E+00	1.23E+00	6.50E-02	1.11E-02	2.02E+00	1.23E+00
PRESCHOOL CHILD	1.02E+00	6.24E-01	5.24E-02	6.43E-03	1.03E+00	6.16E-01
CHILD	5.24E-01	3.18E-01	4.04E-02	4.90E-03	5.30E-01	3.13E-01
ADOLESCENT	2.92E-01	1.76E-01	3.01E-02	3.30E-03	3.01E-01	1.74E-01
ADULT	2.46E-01	1.49E-01	2.54E-02	3.07E-03	2.53E-01	1.48E-01

ZONE 1

SILVER	TYPICAL ONTARIO BKG. 100% BACKGROUND		DELORO ALONE (Incremental)		DELORO INCLUDING BACKGROUND (Site plus Bkg.)	
RECEPTOR	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean
INFANT	1.97E+00	1.23E+00	1.35E-02	2.06E-03	1.97E+00	1.22E+00
PRESCHOOL CHILD	1.02E+00	6.24E-01	1.12E-02	1.67E-03	9.87E-01	6.10E-01
CHILD	5.24E-01	3.18E-01	8.36E-03	9.52E-04	4.98E-01	3.09E-01
ADOLESCENT	2.92E-01	1.76E-01	6.22E-03	6.24E-04	2.77E-01	1.71E-01
ADULT	2.46E-01	1.49E-01	5.45E-03	6.07E-04	2.34E-01	1.48E-01

ZONE 2

SILVER	TYPICAL ONTARIO BKG. 100% BACKGROUND		DELORO ALONE (Incremental)		DELORO INCLUDING BACKGROUND (Site plus Bkg.)	
RECEPTOR	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean
INFANT	1.97E+00	1.23E+00	3.33E-02	4.69E-03	1.99E+00	1.23E+00
PRESCHOOL CHILD	1.02E+00	6.24E-01	2.70E-02	3.63E-03	1.00E+00	6.11E-01
CHILD	5.24E-01	3.18E-01	2.07E-02	2.10E-03	5.11E-01	3.10E-01
ADOLESCENT	2.92E-01	1.76E-01	1.54E-02	1.40E-03	2.86E-01	1.72E-01
ADULT	2.46E-01	1.49E-01	1.31E-02	1.32E-03	2.41E-01	1.49E-01

ZONE 3

SILVER	TYPICAL ONTARIO BKG. 100% BACKGROUND		DELORO ALONE (Incremental)		DELORO INCLUDING BACKGROUND (Site plus Bkg.)	
RECEPTOR	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean
INFANT	1.97E+00	1.23E+00	6.60E-02	1.40E-02	2.02E+00	1.24E+00
PRESCHOOL CHILD	1.02E+00	6.24E-01	5.32E-02	1.06E-02	1.03E+00	6.18E-01
CHILD	5.24E-01	3.18E-01	4.11E-02	6.18E-03	5.31E-01	3.14E-01
ADOLESCENT	2.92E-01	1.76E-01	3.06E-02	4.17E-03	3.01E-01	1.75E-01
ADULT	2.46E-01	1.49E-01	2.57E-02	3.87E-03	2.54E-01	1.51E-01

ZONE 4

SILVER	TYPICAL ONTARIO BKG. 100% BACKGROUND		DELORO ALONE (Incremental)		DELORO INCLUDING BACKGROUND (Site plus Bkg.)	
RECEPTOR	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean
INFANT	1.97E+00	1.23E+00	6.60E-02	1.40E-02	2.02E+00	1.24E+00
PRESCHOOL CHILD	1.02E+00	6.24E-01	5.32E-02	1.06E-02	1.03E+00	6.18E-01
CHILD	5.24E-01	3.18E-01	4.11E-02	6.18E-03	5.31E-01	3.14E-01
ADOLESCENT	2.92E-01	1.76E-01	3.06E-02	4.17E-03	3.01E-01	1.75E-01
ADULT	2.46E-01	1.49E-01	2.57E-02	3.87E-03	2.54E-01	1.51E-01

TRESPASSER SCENARIO

Trespassing Only

Whole Town

ARSENIC	TYPICAL ONTARIO BKG (100% bkg)				DELORO ALONE (incremental)				DELORO INCLUDING BKG (site + Bkg)			
RECEPTOR	Plausible max	mean	5th %	95th %	Plausible max	mean	5th %	95th %	Plausible max	mean	5th %	95th %
INFANT	2.62E-05	6.27E-06	NA	NA	3.49E-05	2.39E-06	NA	NA	5.95E-05	8.33E-06	NA	NA
PRESCHOOL CHILD	1.99E-04	2.96E-05	NA	NA	1.65E-04	1.21E-05	NA	NA	3.50E-04	3.90E-05	NA	NA
CHILD	2.87E-04	2.38E-05	NA	NA	1.75E-04	1.30E-05	NA	NA	4.47E-04	3.47E-05	NA	NA
ADOLESCENT	2.08E-04	3.00E-05	NA	NA	1.24E-04	5.77E-06	NA	NA	3.21E-04	3.44E-05	NA	NA
ADULT	6.93E-04	1.64E-04	NA	NA	7.24E-04	3.26E-05	NA	NA	1.34E-03	1.87E-04	NA	NA
COMPOSITE	1.41E-03	2.53E-04	NA	NA	6.15E-04	6.58E-05	NA	NA	1.91E-03	3.03E-04	NA	NA

Whole Town

ARSENIC	TYPICAL ONTARIO BKG (100% bkg)				DELORO ALONE (incremental)				DELORO INCLUDING BKG (site + Bkg)			
RECEPTOR	Plausible max	mean	5th %	95th %	Plausible max	mean	5th %	95th %	Plausible max	mean	5th %	95th %
INFANT	8.08E+00	1.95E+00	NA	NA	1.09E+01	7.45E-01	NA	NA	1.85E+01	2.59E+00	NA	NA
PRESCHOOL CHILD	6.76E+00	1.01E+00	NA	NA	5.71E+00	4.18E-01	NA	NA	1.21E+01	1.35E+00	NA	NA
CHILD	6.28E-06	5.20E-01	NA	NA	3.89E+00	2.88E-01	NA	NA	9.92E+00	7.67E-01	NA	NA
ADOLESCENT	3.99E+00	5.77E-01	NA	NA	2.42E+00	1.12E-01	NA	NA	6.24E+00	6.66E-01	NA	NA
ADULT	2.11E+00	5.05E-01	NA	NA	2.25E+00	1.01E-01	NA	NA	4.17E+00	5.79E-01	NA	NA
COMPOSITE	0.00E+00	0.00E+00	NA	NA	0.00E+00	0.00E+00	NA	NA	0.00E+00	0.00E+00	NA	NA

NON-CARCINOGENIC

TRESPASSER SCENARIO

Trespassing only

Whole Town

COBALT RECEPTOR	TYPICAL ONTARIO BKG. 100% BACKGROUND		DELORO ALONE (Incremental)		DELORO INCLUDING BACKGROUND (Site plus Bkg.)	
	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean
INFANT	1.82E+00	9.45E-01	4.96E-02	8.86E-03	5.40E-01	3.09E-01
PRESCHOOL CHILD	3.51E+00	1.20E+00	1.84E-02	4.49E-03	5.87E-01	2.45E-01
CHILD	2.50E+00	9.07E-01	9.32E-03	2.89E-03	3.87E-01	3.37E-01
ADOLESCENT	1.56E+00	5.44E-01	2.66E-03	5.06E-04	2.34E-01	2.44E-01
ADULT	1.30E+00	4.59E-01	3.00E-03	4.29E-04	1.95E-01	2.06E-01

TRESPASSER SCENARIO

Trespassing only

Whole Town

LEAD	TYPICAL ONTARIO BKG (100% bkg)				DELORO ALONE (incremental)				DELORO INCLUDING BKG (site + Bkg)			
RECEPTOR	Plausible max	mean	5th %	95th %	Plausible max	mean	5th %	95th %	Plausible max	mean	5th %	95th %
INFANT	2.48E+00	9.86E-01	NA	NA	3.22E-01	9.20E-02	NA	NA	1.29E+00	8.68E-01	NA	NA
PRESCHOOL CHILD	2.55E+00	9.13E-01	NA	NA	1.19E-01	4.59E-02	NA	NA	1.30E+00	8.06E-01	NA	NA
CHILD	1.57E+00	5.97E-01	NA	NA	5.99E-02	2.94E-02	NA	NA	8.39E-01	5.55E-01	NA	NA
ADOLESCENT	1.06E+00	3.71E-01	NA	NA	1.70E-02	4.79E-03	NA	NA	5.24E-01	3.44E-01	NA	NA
ADULT	1.19E+00	4.25E-01	NA	NA	1.93E-02	4.06E-03	NA	NA	5.55E-01	3.92E-01	NA	NA

TRESPASSER SCENARIO

Trespassing only

Whole Town

NICKEL RECEPTOR	TYPICAL ONTARIO BKG. 100% BACKGROUND		DELORO ALONE (Incremental)		DELORO INCLUDING BACKGROUND (Site plus Bkg.)	
	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean	Plausible Max.	Typical Mean
INFANT	2.44E+01	2.05E+01	1.16E+00	2.02E-01	1.90E+01	1.76E+01
PRESCHOOL CHILD	2.81E+01	1.77E+01	4.42E-01	1.04E-01	1.46E+01	1.31E+01
CHILD	1.90E+01	1.18E+01	2.29E-01	6.81E-02	9.28E+00	9.07E+00
ADOLESCENT	1.15E+01	6.87E+00	7.34E-02	1.54E-02	5.31E+00	5.39E+00
ADULT	9.31E+00	5.49E+00	7.99E-02	1.35E-02	4.18E+00	4.24E+00

TRESPASSER SCENARIO

Trespassing only

Whole Town

SILVER RECEPTOR	TYPICAL ONTARIO BKG. 100% BACKGROUND Plausible Max.	 Typical Mean	DELORO ALONE (Incremental) Plausible Max.	 Typical Mean	DELORO INCLUDING BACKGROUND (Site plus Bkg.) Plausible Max.	 Typical Mean
INFANT	1.97E+00	1.23E+00	5.28E-02	4.90E-03	2.01E+00	1.23E+00
PRESCHOOL CHILD	1.02E+00	6.24E-01	3.16E-02	3.28E-03	1.01E+00	6.11E-01
CHILD	5.24E-01	3.18E-01	2.31E-02	2.48E-03	5.13E-01	3.10E-01
ADOLESCENT	2.92E-01	1.76E-01	1.59E-02	1.59E-03	2.86E-01	1.72E-01
ADULT	2.46E-01	1.49E-01	1.46E-02	1.45E-03	2.43E-01	1.46E-01

Typical Ontario Background Scenario — *ARSENIC*

VILLAGE CONCENTRATIONS

	max	mean		max	mean		max	mean
Outdoor Air Concentrations (µg/m3)	2.45E-04	1.00E-04	Municiple Supply (ug/L)	3.56E+00	3.56E+00	Soil Concentration (ug/g)	3.08E+02	1.11E+02
Indoor Air Concentration (µg/m3)	1.84E-04	7.50E-05	Well Water (µg/L)	3.56E+00	3.56E+00	Indoor dust Concentration (ug/g)	1.20E+02	4.34E+01

BACKGROUND CONCENTRATIONS

	max	mean		max	mean		max	mean
Outdoor Air Concentrations (µg/m3)	7.00E-03	1.00E-03	Background supply	1.00E+00	5.00E-01	Soil Concentration (ug/g)	1.70E+01	1.40E+01
Indoor Air Concentration (µg/m3)	5.25E-03	7.50E-04	(ug/L)			Indoor dust Concentration (ug/g)	6.63E+00	5.46E+00

Exposure Limits

	Inhalation	q*	1.30E-02	Oral/Dermal	q* 1.50E-03

Bioavailabilities

	max	mean		max	mean
Inhalation	34.00%	30.00%	Oral/Food	90.00%	90.00%
Study	34.00%	30.00%	Study	95.00%	95.00%

Exposure (µg/kg bw/d)	AP	INFANT		PRESCHOOL CHILD		CHILD		ADOLESCENT		ADULT		COMPOSITE	
Deterministic Scenario		max	mean	max	mean	max	mean	max	mean	max	mean	max	mean
Background Exposure (ug/kg bw/day)													
Outdoor Dust Inhalation	x	1.03E-04	8.55E-06	2.99E-04	1.88E-05	2.16E-04	1.46E-05	1.36E-04	6.77E-06	8.51E-05	7.41E-06	1.18E-04	9.02E-06
Outdoor Soil Ingestion	x	1.64E-02	6.05E-03	9.13E-03	3.01E-03	4.58E-03	1.50E-03	1.26E-03	2.08E-04	1.06E-03	1.75E-04	2.08E-03	5.36E-04
Outdoor Dermal Exposure	x	6.83E-03	1.42E-03	1.10E-02	1.20E-03	9.31E-03	9.83E-04	7.56E-03	8.49E-04	4.67E-03	7.84E-04	5.90E-03	8.42E-04
Indoor Dust Inhalation	x	6.20E-04	5.13E-05	1.30E-03	1.13E-04	9.37E-04	8.79E-05	5.88E-04	5.30E-05	5.14E-04	4.47E-05	6.16E-04	5.44E-05
Indoor Dust Ingestion	x	1.19E-02	3.92E-03	5.90E-03	1.95E-03	2.96E-03	9.73E-04	8.16E-04	1.34E-04	6.89E-04	1.13E-04	1.35E-03	3.47E-04
Indoor Dermal Exposure	x	2.43E-02	3.91E-03	1.99E-02	3.30E-03	1.68E-02	2.71E-03	1.36E-02	2.35E-03	1.29E-02	2.17E-03	1.39E-02	2.33E-03
Drinking Water Exposure	x	7.65E-02	1.74E-02	7.77E-02	1.73E-02	4.50E-02	1.15E-02	3.39E-02	7.96E-03	4.05E-02	1.01E-02	4.29E-02	1.05E-02
Background Home Garden Exposure	x	0.00E+00	0.00E+00	9.77E-03	3.03E-03	7.53E-03	2.30E-03	5.37E-03	1.73E-03	3.99E-03	1.29E-03	4.84E-03	1.55E-03
General Food Basket	x	2.16E+00	5.22E-01	1.80E+00	2.61E-01	1.71E+00	1.31E-01	1.08E+00	1.53E-01	5.40E-01	1.31E-01	8.11E-01	1.44E-01
Inhalation Pathway (Bkg)		7.23E-04	5.98E-05	1.60E-03	1.32E-04	1.15E-03	1.02E-04	7.24E-04	6.17E-05	5.99E-04	5.21E-05	7.34E-04	6.34E-05
Ingestion/Dermal Pathways (Bkg)		2.30E+00	5.55E-01	1.93E+00	2.91E-01	1.80E+00	1.50E-01	1.14E+00	1.66E-01	6.04E-01	1.45E-01	8.82E-01	1.60E-01
Total Bkg Exposure (µg/kg bw/day)		2.30E+00	5.55E-01	1.94E+00	2.91E-01	1.80E+00	1.51E-01	1.14E+00	1.66E-01	6.04E-01	1.45E-01	8.83E-01	1.60E-01
Total Exposure (ug/kg bw/day)													
Inhalation Pathway		7.23E-04	5.98E-05	1.60E-03	1.32E-04	1.15E-03	1.02E-04	7.24E-04	6.17E-05	5.99E-04	5.21E-05	7.34E-04	6.34E-05
Ingestion/Dermal Pathways		2.30E+00	5.55E-01	1.93E+00	2.91E-01	1.80E+00	1.50E-01	1.14E+00	1.66E-01	6.04E-01	1.45E-01	8.82E-01	1.60E-01
Estimated Exposure Ratio (ER)		2.62E+01	6.27E+00	2.00E+02	2.99E+01	2.88E+02	2.42E+01	2.09E+02	3.03E+01	6.97E+02	1.65E+02	1.42E+03	2.56E+02
Predicted Inorganic Urinary Arsenic Level	ug/L	4.72E+01	9.48E+00	5.40E+01	6.76E+00	5.07E+01	3.54E+00	2.93E+01	3.55E+00	1.83E+01	3.67E+00	NA	NA

NOTE:

An Exposure Ratio (ER) of 1.0 is equivalent to a Cancer Risk Level (CRL) of 1 in a million ($1x10^{-6}$).

Typical Deloro Resident - Incremental *ARSENIC*

Whole Town

VILLAGE CONCENTRATIONS

	max	mean		max	mean		max	mean
Outdoor Air Concentrations (µg/m3)	2.45E-04	1.00E-04	Municiple Supply (ug/L)	3.56E+00	3.56E+00	Soil Concentration (ug/g)	3.08E+02	1.11E+02
Indoor Air Concentration (µg/m3)	1.84E-04	7.50E-05	Well Water (µg/L)	3.56E+00	3.56E+00	Indoor dust Concentration (ug/g)	1.20E+02	4.34E+01

BACKGROUND CONCENTRATIONS

	max	mean		max	mean		max	mean
Outdoor Air Concentrations (µg/m3)	7.00E-03	1.00E-03	Background supply	1.00E+00	5.00E-01	Soil Concentration (ug/g)	1.70E+01	1.40E+01
Indoor Air Concentration (µg/m3)	5.25E-03	7.50E-04	(ug/L)			Indoor dust Concentration (ug/g)	6.63E+00	5.46E+00

Exposure Limits

	Inhalation	q*	1.30E-02	Oral/Dermal	q*	1.50E-03

Bioavailabilties

	max	mean		max	mean
Inhalation	34.00%	30.00%	Oral/Food	90.00%	90.00%
Study	34.00%	30.00%	Study	95.00%	95.00%

COMBINED RECEPTOR

Deloro Exposure (µg/kg bw/d)	AP	INFANT		PRESCHOOL CHILD		CHILD		ADOLESCENT		ADULT		COMPOSITE	
Deterministic Scenario		max	mean	max	mean	max	mean	max	mean	max	mean	max	mean
Outdoor Dust Inhalation	x	3.17E-06	7.48E-07	9.18E-06	1.65E-06	6.62E-06	9.80E-07	4.16E-06	5.13E-07	2.62E-06	4.33E-07	2.05E-06	5.77E-07
Outdoor Soil Ingestion	x	2.91E-01	4.20E-02	1.45E-01	2.09E-02	2.25E-02	7.98E-03	2.00E-02	9.62E-04	1.69E-02	8.12E-04	2.28E-02	3.13E-03
Outdoor Dermal Exposure	x	1.40E-01	9.86E-03	1.74E-01	8.34E-03	1.47E-01	5.25E-03	1.20E-01	3.95E-03	7.46E-02	3.65E-03	4.91E-02	4.19E-03
Indoor Dust Inhalation	x	1.90E-05	4.48E-06	3.97E-05	9.86E-06	2.87E-05	5.88E-06	1.80E-05	3.09E-06	1.57E-05	2.61E-06	9.41E-06	3.47E-06
Indoor Dust Ingestion	x	1.88E-01	2.72E-02	9.35E-02	1.35E-02	4.69E-02	5.17E-03	1.29E-02	6.22E-04	1.09E-02	5.25E-04	1.48E-02	2.03E-03
Indoor Dermal Exposure	x	3.85E-01	2.21E-02	3.16E-01	2.29E-02	2.66E-01	1.44E-02	2.16E-01	1.09E-02	2.05E-01	1.00E-02	9.76E-02	1.15E-02
Drinking Water (well water) Exposure													
Drinking Water (municipal supply) Exposure	x	2.44E-01	1.08E-01	2.42E-01	1.08E-01	1.40E-01	5.49E-02	1.06E-01	3.30E-02	1.26E-01	4.16E-02	5.78E-02	4.68E-02
Home Garden Exposure	x	0.00E+00	0.00E+00	6.57E-02	8.96E-03	5.03E-02	6.73E-03	3.56E-02	5.03E-03	2.66E-02	3.78E-03	1.64E-02	4.52E-03
Trespasser-inhalation													
Trespasser-oral													
Trespasser-dermal													
Inhalation Pathway (Site)		2.21E-05	5.23E-06	4.89E-05	1.15E-05	3.53E-05	6.86E-06	2.22E-05	3.60E-06	1.83E-05	3.04E-06	1.15E-05	4.05E-06
Ingestion/Dermal Pathways (Site)		1.25E+00	2.15E-01	1.04E+00	1.82E-01	7.23E-01	9.45E-02	5.09E-01	5.45E-02	4.60E-01	6.06E-02	2.59E-01	7.22E-02
Total Site Exposure (µg/kg bw/day)		1.25E+00	2.15E-01	1.04E+00	1.82E-01	7.23E-01	9.45E-02	5.10E-01	5.45E-02	4.60E-01	6.07E-02	2.59E-01	7.22E-02
Estimated Exposure Ratio (ER)		1.41E+01	2.42E+00	1.05E+02	1.85E+01	1.14E+02	1.49E+01	9.20E+01	9.85E+00	5.19E+02	6.85E+01	4.09E+02	1.14E+02
Predicted Inorganic Urinary Arsenic Level	ug/L	2.56E+01	3.66E+00	2.69E+01	4.24E+00	2.04E+01	2.22E+00	1.30E+01	1.16E+00	1.39E+01	1.53E+00	NA	NA

Typical Deloro Resident (site + background)
Whole Town

ARSENIC

VILLAGE CONCENTRATIONS

		max	mean		max	mean		max	mean
Outdoor Air	Outdoor Air Concentrations (µg/m3)	2.45E-04	1.00E-04	Municiple Supply (ug/L)	3.56E+00	3.56E+00	Soil Concentration (ug/g)	3.08E+02	1.11E+02
Indoor Air C	Indoor Air Concentration (µg/m3)	1.84E-04	7.50E-05	Well Water (µg/L)	3.56E+00	3.56E+00	Indoor dust Concentration (ug/g)	1.20E+02	4.34E+01

BACKGROUND CONCENTRATIONS

		max	mean		max	mean		max	mean
Outdoor Air	Outdoor Air Concentrations (µg/m3)	7.00E-03	1.00E-03	Background supply	1.00E+00	5.00E-01	Soil Concentration (ug/g)	1.70E+01	1.40E+01
Indoor Air C	Indoor Air Concentration (µg/m3)	5.25E-03	7.50E-04	(ug/L)			Indoor dust Concentration (ug/g)	6.63E+00	5.46E+00

Exposure Limits

	Inhalation	q*	1.30E-02	Oral/Dermal	q*	1.50E-03

Bioavailabilities

	max	mean		max	mean
Inhalation	34.00%	30.00%	Oral/Food	90.00%	90.00%
Study	34.00%	30.00%	Study	95.00%	95.00%

COMBINED RECEPTOR

Deloro Exposure (µg/kg bw/d)	AF	INFANT		PRESCHOOL CHILD		CHILD		ADOLESCENT		ADULT		COMPOSITE	
Deterministic Scenario		max	mean	max	mean	max	mean	max	mean	max	mean	max	mean
Outdoor Dust Inhalation	x	3.17E-06	7.48E-07	8.16E-06	1.65E-06	8.62E-06	9.80E-07	4.18E-06	5.13E-07	7.82E-06	4.33E-07	2.05E-06	5.77E-07
Outdoor Soil Ingestion	x	2.91E-01	4.20E-02	1.45E-01	2.09E-02	7.25E-02	7.98E-03	2.00E-02	9.62E-04	1.89E-02	8.12E-04	2.28E-02	3.13E-03
Outdoor Dermal Exposure	x	1.40E-01	9.86E-03	1.74E-01	8.34E-03	1.47E-01	5.25E-03	1.20E-01	3.95E-03	7.48E-02	3.65E-03	4.91E-02	4.19E-03
Indoor Dust Inhalation	x	1.90E-05	4.48E-06	3.97E-05	9.66E-06	2.87E-05	5.86E-06	1.80E-05	3.09E-06	1.57E-05	2.81E-06	9.41E-06	3.47E-06
Indoor Dust Ingestion	x	1.86E-01	2.72E-02	9.35E-02	1.35E-02	4.89E-02	5.17E-03	1.29E-02	8.22E-04	1.09E-02	5.25E-04	1.48E-02	2.03E-03
Indoor Dermal Exposure	x	3.85E-01	2.71E-02	3.18E-01	2.29E-02	2.66E-01	1.44E-02	2.18E-01	1.09E-02	2.05E-01	1.00E-02	9.78E-02	1.15E-02
Drinking Water (well water) Exposure													
Drinking Water (municipal supply) Exposure	x	2.44E-01	1.08E-01	2.42E-01	1.08E-01	1.40E-01	5.49E-02	1.06E-01	3.30E-02	1.26E-01	4.18E-02	5.78E-02	4.66E-02
Home Garden Exposure	x	0.00E+00	0.00E+00	8.57E-02	6.96E-03	5.03E-02	8.73E-03	3.58E-02	5.03E-03	2.66E-02	3.78E-03	1.64E-02	4.52E-03
Trespasser-Inhalation													
Trespasser-oral													
Trespasser-dermal													
Inhalation Pathway (Site)		2.21E-05	5.23E-06	4.89E-05	1.15E-05	3.53E-05	8.88E-06	2.22E-05	3.80E-06	1.83E-05	3.04E-06	1.15E-05	4.05E-06
Ingestion/Dermal Pathways (Site)		1.25E+00	2.15E-01	1.04E+00	1.82E-01	7.23E-01	9.45E-02	5.09E-01	5.45E-02	4.60E-01	8.06E-02	2.59E-01	7.22E-02
Total Site Exposure (µg/kg bw/day)		1.25E+00	2.15E-01	1.04E+00	1.82E-01	7.23E-01	9.45E-02	5.10E-01	5.45E-02	4.60E-01	8.07E-02	2.59E-01	7.22E-02
Background Exposure (ug/kg bw/day)													
Outdoor Dust Inhalation	x	1.29E-05	1.07E-06	3.75E-05	2.35E-06	2.71E-05	4.81E-06	1.70E-05	3.84E-06	1.01E-05	3.07E-06	1.44E-05	3.25E-06
Outdoor Soil Ingestion	x	2.31E-03	7.61E-04	1.14E-03	3.78E-04	5.72E-04	4.96E-04	1.58E-04	8.66E-05	1.33E-04	7.31E-05	2.80E-04	1.42E-04
Outdoor Dermal Exposure	x	1.10E-03	1.77E-04	1.38E-03	1.50E-04	1.17E-03	3.21E-04	9.47E-04	3.52E-04	5.44E-04	3.25E-04	7.10E-04	3.15E-04
Indoor Dust Inhalation	x	7.79E-05	8.45E-06	1.62E-04	1.42E-05	1.17E-04	2.90E-05	7.35E-05	2.21E-05	6.48E-05	1.87E-05	7.73E-05	1.97E-05
Indoor Dust Ingestion	x	1.49E-03	4.92E-04	7.38E-04	2.45E-04	3.70E-04	3.21E-04	1.02E-04	5.60E-05	8.81E-05	4.73E-05	1.68E-04	9.15E-05
Indoor Dermal Exposure	x	3.07E-03	4.93E-04	2.49E-03	4.17E-04	2.10E-03	8.95E-04	1.70E-03	9.62E-04	1.63E-03	9.07E-04	1.75E-03	8.80E-04
Drinking Water Exposure	x	9.66E-03	2.19E-03	9.72E-03	2.17E-03	5.63E-03	3.80E-03	4.24E-03	3.32E-03	5.06E-03	4.20E-03	5.38E-03	3.92E-03
Background Home Garden Exposure													
General Food Basket	x	2.18E+00	5.22E-01	1.80E+00	2.81E-01	1.71E+00	1.31E-01	1.08E+00	1.53E-01	5.40E-01	1.31E-01	8.11E-01	1.44E-01
Inhalation Pathway (Bkg)	x	9.08E-05	7.51E-06	2.00E-04	1.65E-05	1.44E-04	3.38E-05	9.05E-05	2.57E-05	7.47E-05	2.17E-05	9.18E-05	2.30E-05
Ingestion/Dermal Pathways (Bkg)		2.18E+00	5.28E-01	1.82E+00	2.84E-01	1.72E+00	1.38E-01	1.09E+00	1.58E-01	5.47E-01	1.38E-01	8.20E-01	1.50E-01
Total Bkg Exposure (µg/kg bw/day)		2.18E+00	5.28E-01	1.82E+00	2.84E-01	1.72E+00	1.38E-01	1.09E+00	1.58E-01	5.48E-01	1.38E-01	8.20E-01	1.50E-01
Total Exposure (ug/kg bw/day)		3.43E+00	7.41E-01	2.85E+00	4.47E-01	2.44E+00	2.31E-01	1.60E+00	2.12E-01	1.01E+00	1.97E-01	1.08E+00	2.72E-01
Inhalation Pathway		1.13E-04	1.27E-05	2.48E-04	2.80E-05	1.80E-04	4.07E-05	1.13E-04	2.93E-05	9.31E-05	2.48E-05	1.03E-04	2.70E-05
Ingestion/Dermal Pathways		3.43E+00	7.41E-01	2.85E+00	4.47E-01	2.44E+00	2.31E-01	1.60E+00	2.12E-01	1.01E+00	1.97E-01	1.08E+00	2.72E-01
Estimated Exposure Ratio (ER)		3.87E+01	8.38E+00	2.90E+02	4.54E+01	3.88E+02	3.66E+01	2.89E+02	3.84E+01	1.14E+03	2.23E+02	1.71E+03	3.51E+02
Predicted Inorganic Urinary Arsenic Level	ug/L	7.02E+01	1.27E+01	7.95E+01	1.04E+01	8.89E+01	5.42E+00	4.09E+01	4.53E+00	3.05E+01	4.97E+00	NA	NA

Typical Ontario Background Scenario — *ARSENIC*

VILLAGE CONCENTRATIONS

	max	mean		max	mean		max	mean
Outdoor Air Concentrations (ug/m3)	2.45E-04	1.00E-04	Municiple Supply (ug/L)	3.56E+00	3.56E+00	Soil Concentration (ug/g)	3.08E+02	1.11E+02
Indoor Air Concentration (ug/m3)	1.84E-04	7.50E-05	Well Water (ug/L)	3.56E+00	3.56E+00	Indoor dust Concentration (ug/g)	1.20E+02	4.34E+01

BACKGROUND CONCENTRATIONS

	max	mean		max	mean		max	mean
Outdoor Air Concentrations (ug/m3)	7.00E-03	1.00E-03	Background supply (ug/L)	1.00E+00	5.00E-01	Soil Concentration (ug/g)	1.70E+01	1.40E+01
Indoor Air Concentration (ug/m3)	5.25E-03	7.50E-04				Indoor dust Concentration (ug/g)	6.63E+00	5.46E+00

Exposure Limits

Inhalation	q*	1.30E-02	Oral/Dermal	q*	1.50E-03

Bioavailabilities

	max	mean		max	mean
Inhalation	34.00%	30.00%	Oral/Food	90.00%	90.00%
Study	34.00%	30.00%	Study	95.00%	95.00%

COMBINED RECEPTOR

Exposure (ug/kg bw/d)	AP	INFANT		PRESCHOOL CHILD		CHILD		ADOLESCENT		ADULT		COMPOSITE	
Deterministic Scenario		max	mean	max	mean	max	mean	max	mean	max	mean	max	mean
Background Exposure (ug/kg bw/day)													
Outdoor Dust Inhalation	x	1.03E-04	8.55E-06	2.99E-04	1.88E-05	2.16E-04	1.46E-05	1.36E-04	8.77E-06	8.51E-05	7.41E-06	1.18E-04	9.02E-06
Outdoor Soil Ingestion	x	1.84E-02	6.05E-03	9.13E-03	3.01E-03	4.58E-03	1.50E-03	1.26E-03	2.08E-04	1.06E-03	1.75E-04	2.08E-03	5.36E-04
Outdoor Dermal Exposure	x	8.83E-03	1.42E-03	1.10E-02	1.20E-03	9.31E-03	9.83E-04	7.56E-03	8.49E-04	4.67E-03	7.84E-04	5.90E-03	8.42E-04
Indoor Dust Inhalation	x	6.20E-04	5.13E-05	1.30E-03	1.13E-04	9.37E-04	8.79E-05	5.88E-04	5.30E-05	5.14E-04	4.47E-05	6.16E-04	5.44E-05
Indoor Dust Ingestion	x	1.19E-02	3.92E-03	5.90E-03	1.95E-03	2.96E-03	9.73E-04	8.16E-04	1.34E-04	6.89E-04	1.13E-04	1.35E-03	3.47E-04
Indoor Dermal Exposure	x	2.43E-02	3.91E-03	1.99E-02	3.30E-03	1.68E-02	2.71E-03	1.36E-02	2.35E-03	1.29E-02	2.17E-03	1.39E-02	2.33E-03
Drinking Water Exposure	x	7.85E-02	1.74E-02	7.77E-02	1.73E-02	4.50E-02	1.15E-02	3.39E-02	7.96E-03	4.05E-02	1.01E-02	4.29E-02	1.05E-02
Background Home Garden Exposure													
General Food Basket	x	2.16E+00	5.22E-01	1.80E+00	2.61E-01	1.71E+00	1.31E-01	1.08E+00	1.53E-01	5.40E-01	1.31E-01	8.11E-01	1.44E-01
Inhalation Pathway (Bkg)		7.23E-04	5.98E-05	1.60E-03	1.32E-04	1.15E-03	1.02E-04	7.24E-04	6.17E-05	5.99E-04	5.21E-05	7.34E-04	6.34E-05
Ingestion/Dermal Pathways (Bkg)		2.30E+00	5.55E-01	1.92E+00	2.88E-01	1.79E+00	1.48E-01	1.14E+00	1.65E-01	6.00E-01	1.44E-01	8.77E-01	1.59E-01
Total Bkg Exposure (ug/kg bw/day)		2.30E+00	5.55E-01	1.93E+00	2.88E-01	1.79E+00	1.48E-01	1.14E+00	1.65E-01	6.00E-01	1.44E-01	8.77E-01	1.59E-01
Total Exposure (ug/kg bw/day)													
Inhalation Pathway		7.23E-04	5.98E-05	1.60E-03	1.32E-04	1.15E-03	1.02E-04	7.24E-04	6.17E-05	5.99E-04	5.21E-05	7.34E-04	6.34E-05
Ingestion/Dermal Pathways		2.30E+00	5.55E-01	1.92E+00	2.88E-01	1.79E+00	1.48E-01	1.14E+00	1.65E-01	6.00E-01	1.44E-01	8.77E-01	1.59E-01
Estimated Exposure Ratio (ER)		2.67E+01	6.27E+00	1.99E+02	2.96E+01	2.87E+02	2.38E+01	2.08E+02	3.00E+01	6.93E+02	1.64E+02	1.41E+03	2.53E+02
Predicted Inorganic Urinary Arsenic Level	ug/L	4.72E+01	9.48E+00	5.37E+01	6.69E+00	5.05E+01	3.48E+00	2.91E+01	3.51E+00	1.82E+01	3.63E+00	NA	NA

Typical Deloro Resident - Incremental *ARSENIC*
Whole Town

VILLAGE CONCENTRATIONS

	max	mean		max	mean		max	mean
Outdoor Air Concentrations (µg/m3)	2 45E-04	1 00E-04	Municiple Supply (ug/L)	3 56E+00	3 56E+00	Soil Concentration (ug/g)	3 08E+02	1 11E+02
Indoor Air Concentration (µg/m3)	1 84E-04	7 50E-05	Well Water (µg/L)	3 56E+00	3 56E+00	Indoor dust Concentration (ug/g)	1 20E+02	4 34E+01

BACKGROUND CONCENTRATIONS

	max	mean		max	mean		max	mean
Outdoor Air Concentrations (µg/m3)	7 00E-03	1 00E-03	Background supply (ug/L)	1 00E+00	5 00E-01	Soil Concentration (ug/g)	1 70E+01	1 40E+01
Indoor Air Concentration (µg/m3)	5 25E-03	7 50E-04				Indoor dust Concentration (ug/g)	6 63E+00	5 46E+00

Exposure Limits

Inhalation	q*	1 30E-02	Oral/Dermal	q*	1 50E-03

Bioavailabilties

	max	mean		max	mean
Inhalation	34 00%	30 00%	Oral/Food	90 00%	90 00%
Study	34 00%	30 00%	Study	95 00%	95 00%

Deloro Exposure (µg/kg bw/d)	CAP	COMBINED RECEPTOR											
		INFANT		PRESCHOOL CHILD		CHILD		ADOLESCENT		ADULT		COMPOSITE	
Deterministic Scenario		max	mean	max	mean	max	mean	max	mean	max	mean	max	mean
Outdoor Dust Inhalation	x	3.17E-06	7.48E-07	9.16E-06	1.65E-06	6.62E-06	9.80E-07	4.16E-06	5.13E-07	2.62E-06	4.33E-07	2.05E-06	5.77E-07
Outdoor Soil Ingestion	x	2.91E-01	4.20E-02	1.45E-01	2.09E-02	7.25E-02	7.98E-03	2.00E-02	9.62E-04	1.69E-02	8.12E-04	2.28E-02	3.13E-03
Outdoor Dermal Exposure	x	1.40E-01	9.86E-03	1.74E-01	8.34E-03	1.47E-01	5.25E-03	1.20E-01	3.95E-03	7.46E-02	3.65E-03	4.91E-02	4.19E-03
Indoor Dust Inhalation	x	1.90E-05	4.48E-06	3.97E-05	9.86E-06	2.87E-05	5.88E-06	1.80E-05	3.09E-06	1.57E-05	2.61E-06	9.41E-06	3.47E-06
IndoorDust Ingestion	x	1.88E-01	2.72E-02	9.35E-02	1.35E-02	4.69E-02	5.17E-03	1.29E-02	6.22E-04	1.09E-02	5.25E-04	1.48E-02	2.03E-03
Indoor Dermal Exposure	x	3.85E-01	2.71E-02	3.16E-01	2.29E-02	2.66E-01	1.44E-02	2.16E-01	1.09E-02	2.05E-01	1.00E-02	9.76E-02	1.15E-02
Drinking Water (well water) Exposure													
Drinking Water (municipal supply) Exposure	x	2.44E-01	1.08E-01	2.42E-01	1.08E-01	1.40E-01	5.49E-02	1.06E-01	3.30E-02	1.26E-01	4.18E-02	5.78E-02	4.68E-02
Home Garden Exposure													
Trespasser-Inhalation													
Trespasser-oral													
Trespasser-dermal													
Inhalation Pathway (Site)		2.21E-05	5.23E-06	4.89E-05	1.15E-05	3.53E-05	6.86E-06	2.22E-05	3.60E-06	1.83E-05	3.04E-06	1.15E-05	4.05E-06
Ingestion/Dermal Pathways (Site)		1.25E+00	2.15E-01	9.70E-01	1.73E-01	6.73E-01	8.77E-02	4.74E-01	4.94E-02	4.33E-01	5.69E-02	2.42E-01	6.77E-02
Total Site Exposure (µg/kg bw/day)		1.25E+00	2.15E-01	9.70E-01	1.73E-01	6.73E-01	8.77E-02	4.74E-01	4.95E-02	4.33E-01	5.69E-02	2.42E-01	6.77E-02
Estimated Exposure Ratio (ER)		1.41E+01	2.42E+00	9.86E+01	1.76E+01	1.06E+02	1.39E+01	8.56E+01	8.94E+00	4.89E+02	6.42E+01	3.83E+02	1.07E+02
Predicted Inorganic Urinary Arsenic Level	ug/L	2.56E+01	3.66E+00	2.70E+01	4.03E+00	1.90E+01	2.06E+00	1.21E+01	1.05E+00	1.31E+01	1.44E+00	NA	NA

Typical Deloro Resident (site + background) **ARSENIC**
Whole Town

VILLAGE CONCENTRATIONS

		max	mean		max	mean		max	mean
Outdoor Air	Outdoor Air Concentrations (µg/m3)	2.45E-04	1.00E-04	Municipla Supply (ug/L)	3.56E+00	3.56E+00	Soil Concentration (ug/g)	3.08E+02	1.11E+02
Indoor Air	Indoor Air Concentration (µg/m3)	1.84E-04	7.50E-05	Well Water (µg/L)	3.56E+00	3.56E+00	Indoor dust Concentration (ug/g)	1.20E+02	4.34E+01

BACKGROUND CONCENTRATIONS

		max	mean		max	mean		max	mean
Outdoor Air	Outdoor Air Concentrations (µg/m3)	7.00E-03	1.00E-03	Background supply (ug/L)	1.00E+00	5.00E-01	Soil Concentration (ug/g)	1.70E+01	1.40E+01
Indoor Air	Indoor Air Concentration (µg/m3)	5.25E-03	7.50E-04				Indoor dust Concentration (ug/g)	6.63E+00	5.46E+00

Exposure Limits

	Inhalation	q*	1.30E-02	Oral/Dermal	q*	1.50E-03
Bioavailabilities		max	mean		max	mean
	Inhalation	34.00%	30.00%	Oral/Food	90.00%	90.00%
	Study	34.00%	30.00%	Study	95.00%	95.00%

Deloro Exposure (µg/kg bw/d)	AP	COMBINED RECEPTOR											
		INFANT		PRESCHOOL CHILD		CHILD		ADOLESCENT		ADULT		COMPOSITE	
Deterministic Scenario		max	mean	max	mean	max	mean	max	mean	max	mean	max	mean
Outdoor Dust Inhalation	x	3.17E-06	7.48E-07	9.18E-06	1.85E-06	6.62E-06	9.60E-07	4.16E-06	5.13E-07	2.62E-06	4.33E-07	2.05E-06	5.77E-07
Outdoor Soil Ingestion	x	2.91E-01	4.20E-02	1.45E-01	2.09E-02	7.25E-02	7.98E-03	2.00E-02	9.62E-04	1.69E-02	8.12E-04	2.28E-02	3.13E-03
Outdoor Dermal Exposure	x	1.40E-01	9.86E-03	1.74E-01	8.34E-03	1.47E-01	5.25E-03	1.20E-01	2.95E-03	2.46E-02	3.85E-03	4.91E-02	4.19E-03
Indoor Dust Inhalation	x	1.90E-05	4.48E-06	3.97E-05	9.86E-06	2.87E-05	5.68E-06	1.60E-05	3.09E-06	1.57E-05	2.81E-06	9.41E-06	3.47E-06
Indoor Dust Ingestion	x	1.68E-01	2.72E-02	9.35E-02	1.35E-02	4.69E-02	5.17E-03	1.29E-02	6.22E-04	1.09E-02	5.25E-04	1.48E-02	2.03E-03
Indoor Dermal Exposure	x	3.85E-01	2.71E-02	3.16E-01	2.29E-02	2.66E-01	1.44E-02	2.18E-01	1.09E-02	2.05E-01	1.00E-02	9.76E-02	1.15E-02
Drinking Water (well water) Exposure	x	2.44E-01	1.08E-01	2.42E-01	1.08E-01	1.40E-01	5.49E-02	1.06E-01	3.30E-02	1.26E-01	4.16E-02	5.78E-02	4.68E-02
Drinking Water (municipal supply) Exposure													
Home Garden Exposure													
Trespasser-Inhalation													
Trespasser-oral													
Trespasser-dermal													
Inhalation Pathway (Site)		2.21E-05	5.23E-06	4.89E-05	1.15E-05	3.53E-05	8.86E-06	2.22E-05	3.60E-06	1.63E-05	3.04E-06	1.15E-05	4.05E-06
Ingestion/Dermal Pathways (Site)		1.25E+00	2.15E-01	9.70E-01	1.73E-01	8.73E-01	8.77E-02	4.74E-01	4.94E-02	4.33E-01	5.89E-02	2.42E-01	8.77E-02
Total Site Exposure (µg/kg bw/day)		1.25E+00	2.15E-01	9.70E-01	1.73E-01	8.73E-01	8.77E-02	4.74E-01	4.95E-02	4.33E-01	5.89E-02	2.42E-01	8.77E-02
Background Exposure (ug/kg bw/day)													
Outdoor Dust Inhalation	x	1.29E-05	1.07E-06	3.75E-05	2.35E-06	2.71E-05	4.81E-06	1.70E-05	3.64E-06	1.01E-05	3.07E-06	1.44E-05	3.25E-06
Outdoor Soil Ingestion	x	2.31E-03	7.61E-04	1.14E-03	3.78E-04	5.72E-04	4.96E-04	1.58E-04	8.66E-05	1.33E-04	7.31E-05	2.60E-04	1.42E-04
Outdoor Dermal Exposure	x	1.10E-03	1.77E-04	1.38E-03	1.50E-04	1.17E-03	3.21E-04	9.47E-04	3.52E-04	5.44E-04	3.25E-04	7.10E-04	3.15E-04
Indoor Dust Inhalation	x	7.79E-05	8.45E-06	1.62E-04	1.42E-05	1.17E-04	2.90E-05	7.35E-05	2.21E-05	6.46E-05	1.87E-05	7.73E-05	1.97E-05
Indoor Dust Ingestion	x	1.49E-03	4.92E-04	7.36E-04	2.45E-04	3.70E-04	3.21E-04	1.02E-04	5.60E-05	8.61E-05	4.73E-05	1.68E-04	9.15E-05
Indoor Dermal Exposure	x	3.07E-03	4.93E-04	2.49E-03	4.17E-04	2.10E-03	8.95E-04	1.70E-03	9.82E-04	1.63E-03	9.07E-04	1.75E-03	8.80E-04
Drinking Water Exposure	x	9.86E-03	2.19E-03	9.72E-03	2.17E-03	5.63E-03	3.60E-03	4.24E-03	3.32E-03	5.06E-03	4.20E-03	5.36E-03	3.92E-03
Background Home Garden Exposure													
General Food Basket	x	2.18E+00	5.22E-01	1.60E+00	2.81E-01	1.71E+00	1.31E-01	1.08E+00	1.53E-01	5.40E-01	1.31E-01	8.11E-01	1.44E-01
Inhalation Pathway (Bkg)	x	9.08E-05	7.51E-06	2.00E-04	1.65E-05	1.44E-04	3.38E-05	9.05E-05	2.57E-05	7.47E-05	2.17E-05	9.16E-05	2.30E-05
Ingestion/Dermal Pathways (Bkg)		2.18E+00	5.26E-01	1.62E+00	2.84E-01	1.72E+00	1.36E-01	1.09E+00	1.58E-01	5.47E-01	1.36E-01	8.20E-01	1.50E-01
Total Bkg Exposure (µg/kg bw/day)		2.18E+00	5.26E-01	1.62E+00	2.84E-01	1.72E+00	1.36E-01	1.09E+00	1.58E-01	5.47E-01	1.36E-01	8.20E-01	1.50E-01
Total Exposure (ug/kg bw/day)		3.43E+00	7.41E-01	2.79E+00	4.38E-01	2.39E+00	2.24E-01	1.56E+00	2.07E-01	9.81E-01	1.93E-01	1.06E+00	2.17E-01
Inhalation Pathway		1.13E-04	1.27E-05	2.48E-04	2.80E-05	1.80E-04	4.07E-05	1.13E-04	2.93E-05	9.31E-05	2.48E-05	1.03E-04	2.70E-05
Ingestion/Dermal Pathways		3.43E+00	7.41E-01	2.79E+00	4.38E-01	2.39E+00	2.24E-01	1.56E+00	2.07E-01	9.81E-01	1.93E-01	1.06E+00	2.17E-01
Estimated Exposure Ratio (ER)		3.67E+01	8.36E+00	2.83E+02	4.45E+01	3.79E+02	3.58E+01	2.82E+02	3.75E+01	1.11E+03	2.18E+02	1.68E+03	3.44E+02
Predicted Inorganic Urinary Arsenic Level	ug/L	7.02E+01	1.27E+01	7.77E+01	1.02E+01	8.75E+01	5.27E+00	3.99E+01	4.42E+00	2.97E+01	4.87E+00	NA	NA

Typical Deloro Resident - Incremental — *ARSENIC*

Whole Town

VILLAGE CONCENTRATIONS

	max	mean		max	mean		max	mean
Outdoor Air Concentrations (µg/m3)	2 45E-04	1 00E-04	Municiple Supply (ug/L)	3 56E+00	3 56E+00	Soil Concentration (ug/g)	3 08E+02	1 11E+02
Indoor Air Concentration (µg/m3)	1 84E-04	7 50E-05	Well Water (µg/L)	3 56E+00	3 56E+00	Indoor dust Concentration (ug/g)	1 20E+02	4 34E+01

BACKGROUND CONCENTRATIONS

	max	mean		max	mean		max	mean
Outdoor Air Concentrations (µg/m3)	7 00E-03	1 00E-03	Background supply	1 00E+00	5 00E-01	Soil Concentration (ug/g)	1 70E+01	1 40E+01
Indoor Air Concentration (µg/m3)	5 25E-03	7 50E-04	(ug/L)			Indoor dust Concentration (ug/g)	6 63E+00	5 46E+00

Exposure Limits

Inhalation	q*	1 30E-02	Oral/Dermal	q*	1 50E-03

Bioavailabilties

	max	mean		max	mean
Inhalation	34 00%	30 00%	Oral/Food	90 00%	90 00%
Study	34 00%	30 00%	Study	95 00%	95 00%

		COMBINED RECEPTOR											
Deloro Exposure (µg/kg bw/d)	AP	INFANT		PRESCHOOL CHILD		CHILD		ADOLESCENT		ADULT		COMPOSITE	
Deterministic Scenario		max	mean	max	mean	max	mean	max	mean	max	mean	max	mean
Outdoor Dust Inhalation	x	2 78E-06	6 57E-07	8 32E-06	1 45E-06	6 01E-06	6 22E-07	3 77E-06	4 19E-07	2 30E-06	3 53E-07	1 85E-06	4 80E-07
Outdoor Soil Ingestion	x	2 87E-01	4 15E-02	1 43E-01	2 06E-02	7 15E-02	7 84E-03	1 97E-02	9 42E-04	1 66E-02	7 96E-04	2 25E-02	3 08E-03
Outdoor Dermal Exposure	x	1 25E-01	8 78E-03	1 61E-01	7 42E-03	1 36E-01	4 50E-03	1 11E-01	3 30E-03	8 65E-02	3 05E-03	4 51E-02	3 54E-03
Indoor Dust Inhalation	x	1 90E-05	4 48E-06	3 97E-05	9 86E-06	2 87E-05	5 88E-06	1 80E-05	3 09E-06	1 57E-05	2 61E-06	9 41E-06	3 47E-06
Indoor Dust Ingestion	x	1 86E-01	2 68E-02	9 22E-02	1 33E-02	4 63E-02	5 07E-03	1 27E-02	6 09E-04	1 08E-02	5 15E-04	1 46E-02	1 99E-03
Indoor Dermal Exposure	x	3 85E-01	2 71E-02	3 16E-01	2 29E-02	2 66E-01	1 44E-02	2 16E-01	1 09E-02	2 05E-01	1 00E-07	9 76E-02	1 15E-02
Drinking Water (well water) Exposure													
Drinking Water (municipal supply) Exposure	x	2 44E-01	1 08E-01	2 42E-01	1 08E-01	1 40E-01	5 49E-02	1 06E-01	3 30E-02	1 26E-01	4 18E-07	5 78E-02	4 68E-02
Home Garden Exposure	x	0 00E+00	0 00E+00	8 57E-02	8 96E-03	5 03E-02	6 73E-03	3 56E-02	5 03E-03	2 66E-02	3 78E-03	1 64E-02	4 52E-03
Trespasser-Inhalation	x	3 21E-07	1 55E-07	7 00E-07	3 42E-07	5 06E-07	2 68E-07	3 18E-07	1 61E-07	2 66E-07	1 36E-07	1 65E-07	1 65E-07
Trespasser-oral	x	2 12E+00	1 73E-01	2 77E-01	6 62E-02	3 90E-01	5 50E-02	1 07E-01	8 54E-03	1 23E-01	7 21E-03	1 30E-01	1 84E-02
Trespasser-dermal	x	9 75E-01	3 89E-02	8 52E-01	3 29E-02	7 18E-01	2 72E-02	5 83E-01	2 35E-02	5 19E-01	2 17E-07	2 59E-01	2 33E-02
Inhalation Pathway (Site)		2 21E-05	5 29E-06	4 87E-05	1 16E-05	3 52E-05	6 97E-06	7 21E-05	3 67E-06	1 83E-05	3 10E-06	1 14E-05	4 11E-06
Ingestion/Dermal Pathways (Site)		4 32E+00	4 25E-01	2 65E+00	3 00E-01	1 87E+00	1 76E-01	1 19E+00	8 58E-02	1 09E+00	8 89E-02	6 44E-01	1 13E-01
Total Site Exposure (µg/kg bw/day)		4 32E+00	4 25E-01	2 65E+00	3 00E-01	1 82E+00	1 76E-01	1 19E+00	8 58E-02	1 09E+00	8 89E-02	6 44E-01	1 13E-01
Estimated Exposure Ratio (ER)		4 87E+01	4 79E+00	2 69E+02	3 05E+01	2 87E+02	2 78E+01	2 15E+02	1 55E+01	1 73E+03	1 00E+02	1 02E+03	1 79E+07
Predicted Inorganic Urinary Arsenic Level	ug/L	6 86E+01	7 26E+00	7 38E+01	6 97E+00	5 13E+01	4 13E+00	3 04E+01	1 83E+00	3 31E+01	2 24E+00	NA	NA

Typical Deloro Resident (site + background) — *ARSENIC*

Whole Town

VILLAGE CONCENTRATIONS

		max	mean		max	mean		max	mean
Outdoor Air	Outdoor Air Concentrations (ug/m3)	2.45E-04	1.00E-04	Municiple Supply (ug/L)	3.56E+00	3.56E+00	Soil Concentration (ug/g)	3.08E+02	1.11E+02
Indoor Air	Indoor Air Concentration (ug/m3)	1.84E-04	7.50E-05	Well Water (ug/L)	3.56E+00	3.56E+00	Indoor dust Concentration (ug/g)	1.20E+02	4.34E+01

BACKGROUND CONCENTRATIONS

		max	mean		max	mean		max	mean
Outdoor Air	Outdoor Air Concentrations (ug/m3)	7.00E-03	1.00E-03	Background supply	1.00E+00	5.00E-01	Soil Concentration (ug/g)	1.70E+01	1.40E+01
Indoor Air	Indoor Air Concentration (ug/m3)	5.25E-03	7.50E-04	(ug/L)			Indoor dust Concentration (ug/g)	6.63E+00	5.46E+00

Exposure Limits

	Inhalation	q*	1.30E-02	Oral/Dermal	q*	1.50E-03
Bioavailabilities		max	mean		max	mean
	Inhalation	34.00%	30.00%	Oral/Food	90.00%	90.00%
	Study	34.00%	30.00%	Study	95.00%	95.00%

Deloro Exposure (ug/kg bw/d)	AP	COMBINED RECEPTOR											
		INFANT		PRESCHOOL CHILD		CHILD		ADOLESCENT		ADULT		COMPOSITE	
Deterministic Scenario		max	mean	max	mean	max	mean	max	mean	max	mean	max	mean
Outdoor Dust Inhalation	X	2.78E-06	6.57E-07	6.32E-06	1.45E-06	6.01E-06	6.22E-07	3.77E-06	4.19E-07	2.30E-06	3.53E-07	1.65E-06	4.80E-07
Outdoor Soil Ingestion	X	2.87E-01	4.15E-02	1.43E-01	2.06E-02	7.15E-02	7.84E-03	1.97E-02	9.42E-04	1.66E-02	7.96E-04	2.25E-02	3.08E-03
Outdoor Dermal Exposure	X	1.25E-01	8.78E-03	1.61E-01	2.42E-03	1.38E-01	4.50E-03	1.11E-01	3.30E-03	8.65E-02	3.05E-03	4.51E-02	3.54E-03
Indoor Dust Inhalation	X	1.90E-05	4.48E-06	3.67E-05	8.66E-06	2.87E-05	5.88E-06	1.80E-05	3.09E-06	1.57E-05	2.81E-06	9.41E-06	3.47E-06
Indoor Dust Ingestion	X	1.66E-01	2.68E-02	8.22E-02	1.33E-02	4.63E-02	5.07E-03	1.27E-02	6.09E-04	1.08E-02	5.15E-04	1.48E-02	1.99E-03
Indoor Dermal Exposure	X	3.85E-01	2.71E-02	3.18E-01	2.29E-02	2.86E-01	1.44E-02	2.16E-01	1.09E-02	2.05E-01	1.00E-02	8.78E-02	1.15E-02
Drinking Water (well water) Exposure	X	2.44E-01	1.08E-01	2.42E-01	1.08E-01	1.40E-01	5.49E-02	1.06E-01	2.30E-02	1.28E-01	4.18E-02	5.78E-02	4.68E-02
Drinking Water (municipal supply) Exposure	X	0.00E+00	0.00E+00	6.57E-02	8.96E-03	5.03E-02	6.73E-03	3.58E-02	5.03E-03	2.68E-02	3.78E-03	1.64E-02	4.52E-03
Home Garden Exposure	X	3.21E-07	1.55E-07	7.00E-07	3.42E-07	5.06E-07	2.68E-07	3.18E-07	1.61E-07	2.66E-07	1.36E-07	1.85E-07	1.85E-07
Trespasser Inhalation	X	2.12E+00	1.73E-01	7.77E-01	8.62E-02	3.90E-01	5.50E-02	1.07E-01	6.54E-03	1.23E-01	7.21E-03	1.30E-01	1.84E-02
Trespasser oral	X	8.75E-01	3.89E-02	8.52E-01	3.29E-02	7.18E-01	2.72E-02	5.83E-01	2.35E-02	5.19E-01	2.17E-02	2.59E-01	2.33E-02
Trespasser dermal	X	2.21E-05	5.29E-06	4.67E-05	1.16E-05	3.52E-05	6.67E-06	2.21E-05	3.67E-06	1.83E-05	2.10E-06	1.14E-05	4.11E-06
Inhalation Pathway (Site)		4.32E+00	4.25E-01	2.65E+00	3.00E-01	1.82E+00	1.76E-01	1.19E+00	8.58E-02	1.09E+00	8.89E-02	6.44E-01	1.13E-01
Ingestion/Dermal Pathways (Site)		4.22E+00	4.25E-01	2.65E+00	3.00E-01	1.82E+00	1.76E-01	1.19E+00	8.58E-02	1.09E+00	8.89E-02	6.44E-01	1.13E-01
Total Site Exposure (ug/kg bw/day)													
Background Exposure (ug/kg bw/day)													
Outdoor Dust Inhalation	X	1.29E-05	1.07E-06	3.25E-05	2.35E-06	2.71E-05	4.81E-06	1.70E-05	2.84E-06	1.01E-05	3.07E-06	1.44E-05	3.25E-06
Outdoor Soil Ingestion	X	2.31E-03	7.61E-04	1.14E-03	3.78E-04	5.72E-04	4.96E-04	1.58E-04	8.66E-05	1.33E-04	7.31E-05	2.60E-04	1.42E-04
Outdoor Dermal Exposure	X	1.10E-03	1.77E-04	1.38E-03	1.50E-04	1.17E-03	3.21E-04	8.47E-04	3.52E-04	5.44E-04	3.25E-04	7.10E-04	3.15E-04
Indoor Dust Inhalation	X	7.79E-05	8.45E-06	1.62E-04	1.42E-05	1.17E-04	2.90E-05	7.35E-05	2.21E-05	8.46E-05	1.87E-05	2.73E-05	1.97E-05
Indoor Dust Ingestion	X	1.49E-03	4.92E-04	7.38E-04	2.45E-04	3.70E-04	3.21E-04	1.02E-04	5.60E-05	8.61E-05	4.73E-05	1.68E-04	8.15E-05
Indoor Dermal Exposure	X	3.07E-03	4.93E-04	2.49E-03	4.17E-04	2.10E-03	6.95E-04	1.70E-03	9.62E-04	1.63E-03	9.07E-04	1.75E-03	8.80E-04
Drinking Water Exposure	X	9.66E-03	2.19E-03	9.72E-03	2.17E-03	5.63E-03	3.60E-03	4.24E-03	3.32E-03	5.06E-03	4.20E-03	5.36E-03	3.92E-03
Background Home Garden Exposure													
General Food Basket	X	2.16E+00	5.22E-01	1.80E+00	2.61E-01	1.71E+00	1.31E-01	1.08E+00	1.53E-01	5.40E-01	1.31E-01	8.11E-01	1.44E-01
Inhalation Pathway (Bkg)	X	9.08E-05	7.51E-06	2.00E-04	1.65E-05	1.44E-04	3.38E-05	9.05E-05	2.57E-05	7.47E-05	2.17E-05	9.18E-05	2.30E-05
Ingestion/Dermal Pathways (Bkg)		2.18E+00	5.26E-01	1.62E+00	2.84E-01	1.72E+00	1.36E-01	1.09E+00	1.58E-01	5.47E-01	1.36E-01	8.20E-01	1.50E-01
Total Bkg Exposure (ug/kg bw/day)		2.18E+00	5.26E-01	1.62E+00	2.84E-01	1.72E+00	1.36E-01	1.09E+00	1.58E-01	5.47E-01	1.36E-01	8.20E-01	1.50E-01
Total Exposure (ug/kg bw/day)													
Inhalation Pathway		6.50E+00	9.51E-01	4.46E+00	5.64E-01	3.54E+00	3.12E-01	2.26E+00	2.44E-01	1.84E+00	2.25E-01	1.46E+00	2.63E-01
Ingestion/Dermal Pathways		1.13E-04	1.28E-05	2.48E-04	2.62E-05	1.80E-04	4.08E-05	1.13E-04	2.94E-05	9.30E-05	2.48E-05	1.03E-04	2.71E-05
		6.50E+00	9.51E-01	4.46E+00	5.64E-01	3.54E+00	3.12E-01	2.26E+00	2.44E-01	1.84E+00	2.25E-01	1.46E+00	2.63E-01
Estimated Exposure Ratio (ER)		7.33E+01	1.07E+01	4.54E+02	5.74E+01	5.59E+02	4.94E+01	4.11E+02	4.41E+01	1.85E+03	2.54E+02	2.31E+03	4.16E+02
Predicted Inorganic Urinary Arsenic Level	ug/L	1.33E+02	1.82E+01	1.24E+02	1.31E+01	9.86E+01	7.33E+00	5.83E+01	5.19E+00	4.97E+01	5.66E+00	NA	NA

Typical Deloro Resident - Incremental **ARSENIC**

Whole Town

VILLAGE CONCENTRATIONS

	max	mean		max	mean		max	mean
Outdoor Air Concentrations (µg/m3)	2 45E-04	1 00E-04	Municiple Supply (ug/L)	3 56E+00	3 56E+00	Soil Concentration (ug/g)	3 08E+02	1 11E+02
Indoor Air Concentration (µg/m3)	1 84E-04	7 50E-05	Well Water (µg/L)	3 56E+00	3 56E+00	Indoor dust Concentration (ug/g)	1 20E+02	4 34E+01

BACKGROUND CONCENTRATIONS

	max	mean		max	mean		max	mean
Outdoor Air Concentrations (µg/m3)	7 00E-03	1 00E-03	Background supply (ug/L)	1 00E+00	5 00E-01	Soil Concentration (ug/g)	1 70E+01	1 40E+01
Indoor Air Concentration (µg/m3)	5 25E-03	7 50E-04				Indoor dust Concentration (ug/g)	6 63E+00	5 46E+00

Exposure Limits

	Inhalation	q*	1 30E-02	Oral/Dermal	q*	1 50E-03
Bioavailabilties		max	mean		max	mean
	Inhalation	34 00%	30 00%	Oral/Food	90 00%	90 00%
	Study	34 00%	30 00%	Study	95 00%	95 00%

COMBINED RECEPTOR

Deloro Exposure (µg/kg bw/d)	AP	INFANT		PRESCHOOL CHILD		CHILD		ADOLESCENT		ADULT		COMPOSITE	
Deterministic Scenario		max	mean	max	mean	max	mean	max	mean	max	mean	max	mean
Outdoor Dust Inhalation													
Outdoor Soil Ingestion													
Outdoor Dermal Exposure													
Indoor Dust Inhalation													
Indoor Dust Ingestion													
Indoor Dermal Exposure													
Drinking Water (well water) Exposure													
Drinking Water (municipal supply) Exposure													
Home Garden Exposure													
Trespasser-Inhalation	x	3 21E-07	1 55E-07	7 00E-07	3 42E-07	5 06E-07	2 68E-07	3 18E-07	1 61E-07	2 66E-07	1 36E-07	1 65E-07	1 65E-07
Trespasser-oral	x	2 12E+00	1 73E-01	7 77E-01	8 62E-02	3 90E-01	5 50E-02	1 07E-01	8 54E-03	1 23E-01	7 21E-03	1 30E-01	1 84E-02
Trespasser-dermal	x	9 75E-01	3 89E-02	8 52E-01	3 29E-02	7 18E-01	2 72E-02	5 83E-01	2 35E-02	5 19E-01	2 17E-02	2 59E-01	2 33E-02
Inhalation Pathway (Site)		3 21E-07	1 55E-07	7 00E-07	3 42E-07	5 06E-07	2 68E-07	3 18E-07	1 61E-07	2 66E-07	1 36E-07	1 65E-07	1 65E-07
Ingestion/Dermal Pathways (Site)		3 09E+00	2 12E-01	1 63E+00	1 19E-01	1 11E+00	8 22E-02	6 90E-01	3 20E-02	6 42E-01	2 89E-02	3 90E-01	4 17E-02
Total Site Exposure (µg/kg bw/day)		3 09E+00	2 12E-01	1 63E+00	1 19E-01	1 11E+00	8 22E-02	6 90E-01	3 20E-02	6 42E-01	2 89E-02	3 90E-01	4 17E-02
Estimated Exposure Ratio (ER)		3 49E+01	2 39E+00	1 65E+02	1 21E+01	1 75E+02	1 30E+01	1 24E+02	5 77E+00	7 24E+02	3 26E+01	6 15E+02	6 58E+01
Predicted Inorganic Urinary Arsenic Level	ug/L	6 34E+01	3 63E+00	4 54E+01	2 77E+00	3 12E+01	1 93E+00	1 77E+01	6 82E-01	1 94E+01	7 29E-01	NA	NA

Typical Deloro Resident (site + background) — *ARSENIC*

Whole Town

VILLAGE CONCENTRATIONS

		max	mean		max	mean		max	mean
Outdoor Air	Outdoor Air Concentrations (µg/m3)	2.45E-04	1.00E-04	Municipla Supply (ug/L)	3.56E+00	3.56E+00	Soil Concentration (ug/g)	3.08E+02	1.11E+02
Indoor Air C	Indoor Air Concentration (µg/m3)	1.64E-04	7.50E-05	Well Water (µg/L)	3.56E+00	3.56E+00	Indoor dust Concentration (ug/g)	1.20E+02	4.34E+01

BACKGROUND CONCENTRATIONS

		max	mean		max	mean		max	mean
Outdoor Air	Outdoor Air Concentrations (µg/m3)	7.00E-03	1.00E-03	Background supply	1.00E+00	5.00E-01	Soil Concentration (ug/g)	1.70E+01	1.40E+01
Indoor Air C	Indoor Air Concentration (µg/m3)	5.25E-03	7.50E-04	(ug/L)			Indoor dust Concentration (ug/g)	6.63E+00	5.46E+00

Exposure Limits

	Inhalation	q*	1.30E-02	Oral/Dermal	q*	1.50E-03
		max	mean		max	mean
Bioavailabilities	Inhalation	34.00%	30.00%	Oral/Food	90.00%	90.00%
	Study	34.00%	30.00%	Study	95.00%	95.00%

COMBINED RECEPTOR

Deloro Exposure (µg/kg bw/d)	AP	INFANT		PRESCHOOL CHILD		CHILD		ADOLESCENT		ADULT		COMPOSITE	
Deterministic Scenario		max	mean	max	mean	max	mean	max	mean	max	mean	max	mean
Outdoor Dust Inhalation													
Outdoor Soil Ingestion													
Outdoor Dermal Exposure													
Indoor Dust Inhalation													
Indoor Dust Ingestion													
Indoor Dermal Exposure													
Drinking Water (well water) Exposure													
Drinking Water (municipal supply) Exposure													
Home Garden Exposure													
Trespasser-Inhalation	x	3.21E-07	1.55E-07	7.00E-07	3.42E-07	5.08E-07	2.68E-07	3.18E-07	1.61E-07	2.66E-07	1.36E-07	1.85E-07	1.95E-07
Trespasser-oral	x	2.12E+00	1.73E-01	7.77E-01	8.82E-02	3.90E-01	5.50E-02	1.07E-01	8.54E-03	1.23E-01	7.21E-03	1.30E-01	1.84E-02
Trespasser-dermal	x	9.75E-01	3.89E-02	8.52E-01	3.29E-02	7.18E-01	2.72E-02	5.83E-01	2.35E-02	5.19E-01	2.17E-02	2.59E-01	2.33E-02
Inhalation Pathway (Site)	x	3.21E-07	1.55E-07	7.00E-07	3.42E-07	5.06E-07	2.68E-07	3.18E-07	1.61E-07	2.66E-07	1.36E-07	1.85E-07	1.95E-07
Ingestion/Dermal Pathways (Site)	x	3.09E+00	2.12E-01	1.63E+00	1.19E-01	1.11E+00	8.22E-02	8.90E-01	3.20E-02	6.42E-01	2.89E-02	3.90E-01	4.17E-02
Total Site Exposure (µg/kg bw/day)	x	3.09E+00	2.12E-01	1.63E+00	1.19E-01	1.11E+00	8.22E-02	8.90E-01	3.20E-02	6.42E-01	2.89E-02	3.90E-01	4.17E-02
Background Exposure (ug/kg bw/day)													
Outdoor Dust Inhalation	x	1.29E-05	1.07E-06	3.75E-05	2.35E-06	2.71E-05	4.81E-06	1.70E-05	3.64E-06	1.01E-05	3.07E-06	1.44E-05	3.25E-06
Outdoor Soil Ingestion	x	2.31E-03	7.61E-04	1.14E-03	3.78E-04	5.72E-04	4.96E-04	1.58E-04	8.66E-05	1.33E-04	7.31E-05	2.60E-04	1.42E-04
Outdoor Dermal Exposure	x	1.10E-03	1.77E-04	1.38E-03	1.50E-04	1.17E-03	3.21E-04	8.47E-04	3.52E-04	5.44E-04	3.25E-04	7.10E-04	3.15E-04
Indoor Dust Inhalation	x	7.79E-05	8.45E-06	1.82E-04	1.42E-05	1.17E-04	2.90E-05	7.35E-05	2.21E-05	8.48E-05	1.87E-05	7.73E-05	1.07E-05
Indoor Dust Ingestion	x	1.49E-03	4.92E-04	2.38E-04	2.45E-04	3.70E-04	3.21E-04	1.02E-04	5.60E-05	8.61E-05	4.73E-05	1.68E-04	9.15E-05
Indoor Dermal Exposure	x	3.07E-03	4.93E-04	2.49E-03	4.17E-04	2.10E-03	8.95E-04	1.70E-03	9.82E-04	1.63E-03	9.07E-04	1.75E-03	9.80E-04
Drinking Water Exposure	x	9.88E-03	2.19E-03	9.72E-03	2.17E-03	5.63E-03	3.80E-03	4.24E-03	3.32E-03	5.06E-03	4.20E-03	5.36E-03	3.92E-03
Background Home Garden Exposure													
General Food Basket	x	2.18E+00	5.22E-01	1.60E+00	2.81E-01	1.71E+00	1.31E-01	1.08E+00	1.53E-01	5.40E-01	1.31E-01	8.11E-01	1.44E-01
Inhalation Pathway (Bkg)	x	9.08E-05	7.51E-06	2.00E-04	1.65E-05	1.44E-04	3.38E-05	9.05E-05	2.57E-05	7.47E-05	2.17E-05	9.16E-05	2.30E-05
Ingestion/Dermal Pathways (Bkg)	x	2.18E+00	5.28E-01	1.82E+00	2.64E-01	1.72E+00	1.36E-01	1.09E+00	1.58E-01	5.47E-01	1.36E-01	8.20E-01	1.50E-01
Total Bkg Exposure (µg/kg bw/day)		2.18E+00	5.26E-01	1.82E+00	2.64E-01	1.72E+00	1.36E-01	1.09E+00	1.58E-01	5.48E-01	1.36E-01	8.20E-01	1.50E-01
Total Exposure (ug/kg bw/day)		5.27E+00	7.38E-01	3.44E+00	3.83E-01	2.83E+00	2.19E-01	1.78E+00	1.90E-01	1.19E+00	1.85E-01	1.21E+00	1.91E-01
Inhalation Pathway		9.11E-05	7.67E-06	2.00E-04	1.69E-05	1.45E-04	3.41E-05	9.09E-05	2.59E-05	7.50E-05	2.19E-05	9.18E-05	2.31E-05
Ingestion/Dermal Pathways		5.27E+00	7.38E-01	3.44E+00	3.83E-01	2.83E+00	2.19E-01	1.78E+00	1.90E-01	1.19E+00	1.85E-01	1.21E+00	1.91E-01
Estimated Exposure Ratio (ER)		5.95E+01	8.33E+00	3.50E+02	3.90E+01	4.47E+02	3.47E+01	3.21E+02	3.44E+01	1.34E+03	1.87E+02	1.91E+03	3.03E+02
Predicted Inorganic Urinary Arsenic Level	ug/L	1.08E+02	1.26E+01	9.60E+01	8.91E+00	7.97E+01	5.14E+00	4.55E+01	4.05E+00	3.60E+01	4.18E+00	NA	NA

CANTOX ENVIRONMENTAL

DELORO VILLAGE
EXPOSURE ASSESSMENT AND HEALTH RISK CHARACTERIZATION FOR ARSENIC AND OTHER METALS

APPENDIX D - PEER REVIEW AND RESPONSE

December, 1999

APPENDIX D

RESPONSE TO PEER REVIEW "DELORO VILLAGE EXPOSURE ASSESSMENT AND HEALTH RISK CHARACTERIZATION FOR ARSENIC AND OTHER METALS - DRAFT FOR DISCUSSION"

Responses to comments of the peer reviewers, as follows, have been made only to address those comments pertinent to the work completed by CANTOX ENVIRONMENTAL.

Response to Comments Provided by Dr. Buck Grissom, Centre for Disease Control

Comment 1: Community awareness may affect the results of the study.
With regard to the concern that knowledge regarding concerns on the site may affect the outcome of the biological monitoring, it is felt that the use of risk assessment in addition to the biological monitoring acts as a check mechanism. Because the lack of concern regarding urinary arsenic concentrations is backed up by the results of the exposure modelling and urinary arsenic concentration modelling, there is more confidence in the overall conclusions. It is true that biological monitoring represents a snapshot of exposure, in the case of arsenic, a relatively short term picture of exposures. Again the use of the risk assessment to predict current and future exposures based on the contamination in the village acts as a confirmation of the results of the biological monitoring.
ACTION ITEM: The considerations above will be represented in the discussion/conclusions.

Comment 4b: The soil levels of arsenic in zones 3 and 4 warrant further evaluation. The estimated dose that a 15 kg child would get from soil ingestion (220.8 mg As/kg soil, the median soil arsenic concentration in zone 4) would be approximately $3x10^{-3}$ mg As/kg bw/d (assumptions: 15 kg bw, 200 mg soil ingested/d, median soil arsenic concentration). Adjusting for frequency of exposure (4 months) would result in a dose of $1x10^{-3}$ mg As/kg bw/d. Bioavailability adjustment (0.8) = $8x10^{-4}$ mg As/kg bw/d.

Indoor dust levels may be very important in evaluation exposure and the likelihood that adverse health effects will occur - indoor dust contaminated with hazardous substances has been shown to result in exposures. Indoor dust contaminated with lead, the dust on the hands of children exposed to this dust, and blood lead levels and urine levels of arsenic of these children have been shown to be closely related.

ATSDR's chronic Minimal Risk Level and EPA's chronic oral Reference Dose for arsenic are $3x10^{-4}$ mg/kg/day. Chronic MRLs and RfDs are estimates of the daily exposure of the human population to a chemical that is likely to be without risk of deleterious noncancerous effects during a lifetime. Ingestion of 200 mg soil and dust/day containing 30 mg As/kg soil by a 15 kg child would result in a dose of approximately $3x10^{-4}$ mg As/kg bw/day (assuming 80% absorption the default value used by EPA in Region 8. Mouthing activities by infants, pica behavior by young children, ingestion of sustenance containing arsenic, etc., could result in a substantial increase in the dose of arsenic.

There are several factors that can influence the likelihood that exposure to the levels

of arsenic reported at a site will result in adverse health effects. If the frequency of exposure is reduce, health threats will also be reduced. Frequency of exposure, however, is difficult to evaluate. While people may have less direct contact with contaminated outdoor soil in the winter, they may have greater contact with contaminated indoor dust. Specific subgroups that are susceptible populations may exhibit a different or enhanced response to this metals than will most persons exposure to the same level of this contaminant in the environment. Reasons include genetic makeup, development stage, health and nutritional status, and chemical exposure history. These parameters can result in decreased function of the detoxification and excretory processes (mainly hepatic and renal) or enhance pre-existing compromised function of target organs. For these reasons, the elderly with declining organ function, and the youngest in the population with immature and developing organs will generally be more vulnerable to this substance than healthy adults.

The calculation of potential exposures to adults and children, as conducted by CANTOX ENVIRONMENTAL, involves the use of standard receptor characteristics and the site specific data. The bioavailability factors used in the estimation of uptake from ingestion of soils and dusts are derived from the published, peer-reviewed literature, and are considered to be the most realistic data to use. The use of a bioavailability factor lower than the default value proposed by the U.S. EPA is further supported by the fact that the uptake of arsenic into plants, which was studied within Deloro, would indicate that the arsenic tends to be less bioavailable than might be expected. This means that the specific form of arsenic in the soil is less likely to be taken up through root uptake as well as through biological mechanisms in mammals (e.g., absorption in the gut).
ACTION ITEM: The above considerations will be included in discussion of uncertainties.

It is agreed that indoor dust may present a significant pathway of exposure for children; this is why this pathway was included in the risk assessment for all age groups. The ingestion of soil and dust is greatly affected by individual behaviour, such as children eating dirt or putting dirty objects into their mouths. As discussed in the report, behavioural characteristics are used to represent potential exposures from such pathways; for example, soil ingestion. These data are based on studies in which the soil content of the feces are used to estimate daily soil ingestion from all activities. The two specific values used represent both the upper end of the range (95^{th} percentile) as well as the mean. There are also physiological reasons why specific subgroups may be more susceptible to arsenic exposures; these are discussed in Part 4 of the report, but will be brought forward into the risk assessment discussion as well.
ACTION ITEM: The discussion of susceptible subgroups will be emphasized in the risk assessment report (Part 5) as well as in the toxicity report (Part 4).

Comments 6 through 13 will be responded to in an integrated manner:
Comments 6: Wipe samples provide information concerning the presence or absence of a substance. There are no generally accepted methods for estimating the dose from wipe samples.
Comment 7: The ability of wipe samples to detect substances on carpet or porous surfaces is not good. Particulate substances settle into carpet or crevices where wipes cannot reach

them. Cleaning activities such as vacuuming may redistribute these substances resulting in intermittent exposures.

Comment 9: Vacuum sampling produces date that can be used in standard risk assessments. Vacuum samples are typically collected from a defined area (e.g., 100 cm^2) and expressed as milligrams of contaminant per kilogram dust (mg/kg). Very few people, however have a kilogram of dust in 100 cm^2. Surface load is important in defining amount of the contaminant that a child is likely to contact. According to the USEPA, the concentration of the substance of concern in indoor dust is related to sth source; whereas, the load is more related to human exposure (Sutton, PM, Athanasoulis M, Flessel P, Guirguis G, Haan M, Sclag R, and Goldman LR, 1995. Lead levels in the household environment of children in three high-risk communities in California. Environ Research 68:45-57; and Lanphear BO, Emond M, Jacobs DE, Weitzman M, Tanner M, Winter NL, Yakir B, and Eberly S, 1995. A sisde-by side comparison of dust collection methods for sampling lead-contaminated house dust. Environ Research 68:114-123).

Comment 9a: Wipe samples are not appropriate for sampling carpets and porous surfaces. Furthermore the following reports indicate that indoor lead-contaminated dust may represented health threats.

Comment 10: Frequently, people will clean their homes before indoor dust sampling is conducted; they do not want to be perceived as being unkempt.

Comment 12: Indoor dust concentration (ug/g) may increase after cleanup activities. Dust is a composite of many items including hair, dandruff, lint, soil particles, etc., Cleaning removes these particles at different rates. The load (ug/m^2), however, decreases.

Comment 13: Indoor dustfall is likely to be variable. Factors affecting indoor dustfall include methods and frequency of cleaning (e.g., vacuuming tends to redistribute carpet dust). Indoor transport of contaminates from outdoor sources on shoes, clothing, pets fur, etc. (shoe and lead study, Del Oro arsenic dog fur study, take-home on clothing studies).

It is agreed that swipe samples are not useful in quantifying potential exposures, especially for sampling carpets and porous surfaces. It would be expected based on the presence of arsenic in outdoor air, that there would be exposures in the indoors via dust as well. This is why the exposure assessment for indoor dust was based on relationships between outdoor dust and indoor dust from the published, peer reviewed literature (e.g., Walker and Griffin, 1998 - see Part 5 for full reference). While vacuum data can produce useful data for risk assessment, there are some limitations in using such data which tend to result in an underestimation of potential exposures (for example, not collecting all of the dust in the sample area).

ACTION ITEM: The discussion of indoor dust exposure estimation will be strengthened, including mention of alternate methods, and that generally, there are limitations with all methods of indoor dust sampling and thus difficulties in interpretation, including issues regarding the tendency of homeowners to want to clean house prior to sampling. Given that the methods used to estimate indoor dust exposures are based on actual relationships observed in an intensive U.S. study, it is unlikely that underestimation of such exposure occurred.

Comment 11: If an interpretation of wipe sample data are needed, assume that the amount

reported in a wipe sample is the amount ingested. If the derived dose is less than a health-based guideline such as an RfD or MRL, non-cancerous adverse health effects are not likely to occur. If the dose is greater than the guideline, additional information is needed.
The report already contains a discussion of possible methods whereby the swipe sample data might be used quantitatively, and a comparison of estimates of exposure via these two swipe sample methods versus the soil/dust ratio method (Table 5-3).

Comment 22. A questionnaire asking questions about shellfish consumption may not address ingestion of inorganic arsenic. Shellfish have been shown to contain varying levels of inorganic arsenic.
Consumption patterns for shellfish may be useful in identifying reasons for high total urinary arsenic, and while shellfish may contribute inorganic arsenic to the diet, the majority of arsenic in fish and seafood is in organic forms, and thus do not contribute to inorganic arsenic consumption.

General Comment 1: The appropriateness of extrapolation from information from other sites to the Deloro site depends on similarities and differences among these sites. Exposures to arsenic from sources such as food, water, and soil varies among sites. In Montana, urinary arsenic levels decreased after relocation (CDC [Centers for Disease Control], 1987. Progress in Chronic Disease Prevention Reduction of Children's Arsenic Exposure Following Relocation – Mill Creek, Montana. Morb Mortal Wkly Rep, 36:505-507). More typically, however, biologic monitoring at sites containing arsenic as a contaminant of concern does not indicate elevated urinary arsenic levels. See Comment 1.
The data from other areas in North America are not strictly being extrapolated to the Deloro situation, with the exception of the indoor/outdoor dust calculation described above. This is considered appropriate, as it is based on air dispersion behaviour that is not likely to be affected by soil parameters, etc. The observation of exposure pathways of concern, or mitigation of exposure, or lack thereof, at other mine sites was not used to guide the results of Deloro in any way.

General Comment 2: NHANES data is frequently cited when discussing biologic monitoring data. NHANES data, however, does not address site-specific issues or focus on high-risk populations (Pirkle JL, Brody DJ, Gunter EW, Kramer RA, Paschal DC, Flagal KM, and Matte TD, 1994. The Decline in Blood Lead Levels in the United States: The National Health and Nutrition Examination Survey (NHANES). JAMA 272:284-291).
Agreed, but indications from the Deloro survey would not suggest any unusual patterns of consumption.

Comment 23: Arsenic's mobility depends on factors including the species of arsenic present and the soil type. For most soils, arsenic is not "highly" mobile. A couple of references:

- *Merwin I, Pruyne LPT, Ebel JG Jr, Manzell KL, and Lisk DA, 1994. Persistence, phytotoxicity, and management of arsenic, lead and mercury residues in old orchard soils of New York State. Chemosphere, 29:1361-1367.*
- *Elfving DC, Wilson KR, Ebel JG, Manzell KL, Gutenmann WH, and Lisk DJ, 1994.*

Migration of lead and arsenic in old orchard soils in the Georgian Bay-Region of Ontairo. Chemosphere 29:407-413.

ACTION ITEM: The text will be altered as suggested by the reviewer.

Comment 24: Perhaps. See General Comment 1 concerning exposure to arsenic in soil.
The percent contribution is based on the modelling conducted.

Comment 25: There are several studies involving lead that indicate the soil removal does not have an appreciable effect on blood lead levels indicating that soil ingestion is not a major source of exposure (Thomas L. Schlenker TL, 1993. Soil Abatement and Lead Levels in Children. JAMA, 270:829-830; Weitzman M, Aschengrau A, Bellinger D, Hones R, Hamlin JS, and Beiser A, 1993. Lead-contaminated soil abatement and urban children's blood lead levels. JAMA, 269:1647-1654; Urban Soil Lead Abatement Demonstration Project, Volume 1: EPA Integrated Report. EPA/600/P93/001aF, April 1996. pp:4.19 - 4.25).
Confounder: Differences in protocols among studies

- *Exclusion criteria*
 - ☞ *Children with blood lead levels exceeding 20 - 25 ug/dL were excluded from most studies.*
- *Inclusion criteria*
 - ☞ *Children involved or associated with previous studies have been included in subsequent studies.*
- *Sampling strategies*
 - ☞ *Indoor*
 - *i Dust*

Lead in dust is typically reported as mg Pb/kg dust. The surface load is also important. The amount of lead in an area gives a better indication of the potential for exposure.

ii Carpets

Carpets are difficult to sample. Lead settles into the pile resulting in an underestimation of the amount of lead present.

- *Seasonal differences*
 - ☞ *Summer peaks*
 - ☞ *Winter peaks*

COMMENT 25B: See Comment 4B concerning soil ingestion.

ACTION ITEM: The reviewers comments are well taken, and correspond to the observation that there are no significant increases in exposure between Deloro and typical Ontario residents; the references cited will be incorporated into the discussion of lead exposures in Deloro versus in Ontario.

Comment 26: Most of the arsenic ingested is eliminated in a few days. Arsenic is rapidly excreted; the majority of it is eliminated with 2-3 days; therefore, the length of time between exposure and collection of urine is important. If arsenic is detected in urine, is it the result of a resent exposure to low level of arsenic, a later exposure (e.g., one or two days) to a higher level, or a continuous exposure to an intermediate level. See Comment 1 concerning

community awareness.
We agree that urinary arsenic is an indication of recent exposures, and while a direct relationship between urinary arsenic and health status has not been established, urinary arsenic levels of a chronically exposed population can be very helpful in a weight-of-evidence evaluation of health status (ie., with a risk assessment, cancer incidence evaluation and health survey, as in the current overall study).

Comment 27: Urinary arsenic may not address the health status of a population exposed to arsenic. There are no objective criteria for assessing adverse health effects from low level exposure to arsenic (e.g., 100 ug As/L water). Hypo/hyper pigmentation and dermal karetoses are indicators or appreciable exposure.
It is true that urinary arsenic alone cannot be interpreted with regard to past and future health concerns, and that there are no objective criteria for low level exposures to arsenic, in that even the non-carcinogenic skin changes used as the basis of the non-carcinogenic risk assessment for arsenic, are associated with extreme exposures.
ACTION ITEM: The above will be incorporated into the discussion of arsenic risks, and in collation with biological monitoring results in Part 5.

General Comment 3: The amount of arsenic in urine is variable. Factors such as diluteness, length of time since exposure, species of arsenic ingested, content of the intestinal tract, source of arsenic, environmental distribution of arsenic, etc. can affect the arsenic level reported in urine. See comment 1 concerning awareness and Comment 21 for diluteness.
It is agreed that the diluteness of the urine can affect the concentrations of arsenic. GGI was responsible for evaluation of the urinary arsenic data and has prepared a response to this question. Briefly, first void samples (more likely to be concentrated) were not used. Statistical analysis on a ug/L and a creatinine basis had comparable results, in that no statistically significant differences were seen between Deloro and Havelock residents.
ACTION ITEM: The above will be noted in the results section.

General Comment 4: Herbal medications and teas containing metals including arsenic are becoming more prevalent and can cause elevated urinary arsenic levels and adverse health effects (See attachment 1).
ACTION ITEM: the potential importance of herbal preparations in exposure to arsenic will be discussed in Part 5.

General Comment 5: Estimates of dose exceeding EPA's RfD and ATSDR's MRL are useful as indicators that additional information is needed. Estimated exposures that exceed these reference values does not mean that adverse health effects will occur.
ACTION ITEM: It will be made clear that exposures exceeding the exposure limit are indicators of potential risk, not actual risk of adverse health effects in th general methodology, and Part 5.

General Comment 6: Cancer slope or unit risk factors are useful in indicating that additional information is needed. A weight-of-evidence approach is very useful in assessing the

likelihood that cancer will occur from exposure to arsenic. See the following references:
Inside EPA, 1997.
Ohanian EV, Moore JA, Fowle III Jr, Omenn GS, Lewis SC, Gray GM, North DW, 1997. Risk characterization: Abridge to informed decision making. Fund Appl Toxicol, 39:81-88.
Page NP, Aingh DV, FarlandW, Goodman JI, Conolly RB, Andersen ME, Clewell HJ, Frederick CB, Yamasaki H, Lucier G, 1997. Implementation of EPA revised cancer assessment guidelines -
incorporation of mechanistic and pharmacokinetic data. Fund Appl Toxicol, 37:16
Proposed Guidelines for Carcinogen Risk assessment, EPA/600/P-92/003C, April 1996.

It is agreed that a weight of evidence approach provides the most reliable indicator of risk, this will be strengthened in report.

General Comment 7: Rote algorithmic determination (a.k.a., RAD), alone, does not adequately address exposure risks at a site. Probabilistic evaluation may imporve the site assessment; however, the accuracy of sampling data, identification of all sources of arsenic, human behaviours, pets, etc. Detmination of potential threats at a site requires integration of factors such as site-specific information, knowledge of toxicological and medical literature, and an understanding of the strengths and weaknesses of risk assessment procedures. Professional judgement utilizing all available resources is required to reach a conclusion. The knowledge, ability, and professional judgement of risk assessors, health assessors, and health professionals are critical.
General Comment 7a: Comments concerning models from another review for your consideration: Accurate model predictions do not validate a model; likewise, inaccurate model predicitions do not invalidate a model. Practical, scientific, and philosophical problems plague the use of the words "verification and validation" to such an extent that their usage cannot be recommend for either scientific or regulatory purposes. More meaningful descriptors (testing, evaluation, corroboration, analysis) can and should be employed, thereby avoiding the misconception that a model is a "good", "correct", "true," "valid," or "sufficient" representation of reality. Attempts to validate models can result in either model validation being always attainable or always unattainable. Testing models with field or laboratory observations to assess their "validity" is an important aspect of scientific research, but we must remember that it really test their consistency, not necessarily their proximity to truth. In environmental sciences especially, we are always limited by (1) incomplete or inadequate data, (2) our scientific knowledge, and (3) our guide to our thinking and our understanding of the data, but attempts to validate them for regulatory purposes are inappropriate because they lead to misconceptions about scientific and technical capabilities [Dr, D. Kirk Nordstrom, US Geolgical Survey , March 1997]. See Oreskes et al Feb. 4, 1994 and Oreskes et al., April 15, 1994 for additional comments.

The reviewer cites general truisms with regard to probabilistic risk assessment and model validation.

Comment 28: See General Comment 4 concerning medicinals.

Comment 29: Dermal contact, per se, is usually not a primary exposure pathway. Cee General Comment 11.
It is agreed that usually dermal contact is not a significant route of exposure. The bioavailability of metals is relatively low by this route. However, the modelling was designed to provide conservative estimates of exposure, and was based on accepted parameters such as dermal adherence, bioavailability, amount of exposed skin, etc.
ACTION ITEM: The likely overestimation of dermal uptake will be discussed in the uncertainty section.

Comment 30: Current health-based guidelines (e.g., MRLs, RfDs, or RfCs, cancer slope factors) are based on data from data from exposures to arsenic in drinking water in Taiwan. The accuracy of the drinking water data are questionable.
Exposures in food are unknown.
Exposures in air are unknown.
Exposures from dermal contact are unknown (e.g., rice farmers).
Relevance of Taiwan data to U.S. populations is unknown.
Use of Taiwan data to assess adverse health effects in countries such as the U.S. and Canada are questionable. See Attachment 2 (Ken Brown references).
The limitations of the use of Taiwanese data for North American populations are discussed in detail in Part 4, and are in agreement with the comments of the reviewer.
ACTION ITEM: This will be emphasized in the discussion in Part 5.

Comment 31: The inhalation slope factor was derived from occupational exposures and is likely to overestimate non-residential cancer risks. The majority of respirable particles are too large to reach the deep lung areas.
The likely overestimation of cancer risk for arsenic based on occupational studies is well taken.
ACTION ITEM: add consideration re: smaller proportion of particulates in respirable range to Part 4 and to discussion in Part 5.

Comment 32: The oral and inhalation RfDs for lead are interesting. U.S. regulators (e.g., U.S. EPA) and health agencies (ATSDR/CDC) have not developed oral or inhalation guidelines for lead because a threshold has not been identified. CDC's lead guideline is 10 ug/dL (Centers for Disease Control and Prevention, "preventing Lead Poisoning in Young Children,: October 1991). EPA's lead model (IEUBK) estimates blood lead levels from 0.5 1, 1-2, 2-3,...6-7 years of age (Guidance Manual for the Integrated Exposure Uptake Biokinetic Model for Lead in Children; Risk Assessment Guidance for Superfund, Volume I, Human Health Evaluation Manual (Part A) (1989). U.S. EPA and U.S. HUD have developed floor, lower wall, and window lead levels for public housing (sampling House Dust for Lead, Basic Concepts and Literature Review, 1995. EPA 747-R-95-007).

General Comment 8: Bioavailability is an important factor in estimating the likelihood that adverse health effects will occur. There is, however, a problem in using bioavailability because almost all toxicology is expressed as external (or exposure) dose (mg As/kg

BW/day). Lead is a notable exception: lead data are expressed as external dose in some studies and as internal dose in others (ugPb/dL blood). Most toxicological data have been obtained from studies involving ingestion for water soluble forms of arsenic and other metals. The effects of exposure to these substances have been documented. The effects of many species of metals, particularly metals that are not water soluble, have not been adequately evaluated.

Once the relative bioavailability of arsenicals or other metals has been determined, the relative toxicity can be estimated; and the likelihood that adverse health effects will occur can be more accurately estimated. Relative bioavailability, therefore, will facilitate toxicological evaluation of metal compounds with different bioavailabilities.
The adjustment of exposures for bioavailability is correctly done in the risk assessment. Briefly, both the exposure is adjusted for route-specific bioavailability to derive an internal dose, and the exposure limit is likewise adjusted for the route of exposure to an allowable internal dose. The risk characterization is thus conducted by comparing total internal dose to the internal exposure limit for each route of exposure. Rather than employing a relative bioavailability as suggested by the reviewer, CEI simply adjusts both the exposure and hazard criteria by the pertinent factors for use in risk characterization. Numerically the risk characterization would be the same as using a relative bioavailability.
ACTION ITEM: The discussion of bioavailability adjustment will be strengthened in General Methods and in Part 5.

General Comment 9: Chris Weis, Gerry Henninsen, and Susan Griffin (U.S. EPA Region 8) have been conducting arsenic and lead bioavailability studies. Their studies have reported arsenic and lead bioavailability values from soil as high as 60% and 50%, respectively. The U.S. EPA region 8 default bioavailability value for arsenic is 80%.
General Comment 10: The Freeman et al (1993 and 1995) studies clearly indicate that bioavailability of arsenic from dust and soil is not 100%; however, these studies have weaknesses. In the 1993 study, for example, fecal recovery of arsenic after IV injection was 6-10%. Fecal excretion of arsenic, however, may have been underestimated since enterohepatic recirculation of arsenic was not evaluated. Further, only approximately 85% of the administered dose was recovered.
The main source of bioavailability data was the published literature.
ACTION ITEM: The uncertainties associated with the use of the Freeman papers will be discussed in the results section as well as the uncertainty section. As we cannot access or properly reference the values of 50 to 60% cited by the reviewer, we cannot use it in the RA, but we will note this data and discuss the impact on the risk assessment results. It will be noted that increased bioavailability from soil ingestion would increase both the Deloro and typical Ontario exposures, and thus would not likely impact the conclusions of the study. See also response to Comment 4b.

General Comment 11: Dermal absorption of inorganic metals is usually a minor pathway of exposure. Hydrated skin, however, may allow greater dermal penetration than normal (people engaging in work that involved prolonged exposure to water contaminated with

metals). Enhanced uptake of metals through skin may also be enhanced by sweating.
Florence TM, 1998. The absorption of ionic lead compounds through the skin of mice, J nutrit Environ Med, 8:19-23.
Stauber JL, Florence TM, Gulson BL, and Dale LS, 1994. Percutaneous absorption of inorganic lead compounds. Sci Total Environ, 145:55-70.
Lilley SG, Florence TM, and Stauber JL, 1988. The Use of Sweat to Monitor Lead Absorption through the Skin. Sci Total Environ, 76:267-278.

Agreed. See response to comment 29.

General Comments 12: See General Comments 6,7, and 8 for comments concerning arsenic and cancer. Also see Comments 30 and 31.
General Comment 13:.Lung cancers risks are derived from occupational exposures to arsenic. Other cancers risks are derived from Taiwan data. See General Comment 12.
Addressed in preceding comments.

Comment 33: May want to reword the titles to avoid misinterpretation by the public. Suggest something like "Estimated Lifetime..." or "Theoretical Lifetime..."
Agreed.
ACTION ITEM: Wording will be changed to include Estimated Lifetime Cancer Risk on all tables and figures.

Comment 35: Site data indicate that water is not a major contributor (See Deloro Village Exposure Assessment and Health Risk Characterization for Arsenic and Other Metals - Draft for Discussion).
ACTION ITEM: The proportion of overall risks contributed by arsenic will be re-reevaluated in light of the new drinking water concentration data.

Comment 38: How accurate is a 1.2 fold increase considering the uncertainty factors used in the risk assessment methodologies?
Comment 39: See Comment 38.
/General Comment 14: Estimating risks involves using available scientific, medical, and site-specific information. There are always uncertainties (e.g., frequency and duration of exposure, bioavailablility, and quantities of contaminated soil, water, and food ingested, etc. Also see page 5-16). Uncertainty factors are used to account for uncertainties known to exist. A 1.2 fold increased risk implies a preciseness that does not exist (i.e., 1.0 and 1.2 are not real differences; they are only different mathematically). See Comment 38.
Agreed that a 1.2-fold increase cannot be considered significant given the uncertainty factors in the risk assessment, and the conservative assumptions made in various phases of the risk assessment.
ACTION ITEM: The discussion of results will be reworded to more clearly indicate level of risks and the significance of those increases.

General Comment 15: This section's tone implies that lead is a health threat, particularly if

home-grown vegetables are consumed. Table 5.8, however, indicates that risks are minimal. Probabilistic 95% risks range from 0.53 to 2.59 (see General Comment 14 and Comment 39).
General Comment 15b: The lead levels reported in soil have not been shown to produce problems in garden vegetables (Chaney etal; Sterrett et al; etc).
Agreed. The estimated exposure to lead from consumption of home garden produce slightly increases overall risk, but does not significantly impact risks.
ACTION ITEM: The discussion of pathways analysis, significance of home garden will more clearly state the above, and studies such as those cited by the reviewer will be incorporated.

Comment 43: Models may overestimate because of model failure to account for site-specific variables including community awareness. See Comment 1 and General Comment 7a.
Agreed.
ACTION ITEM: possibility of altered community behaviour (which would reduce actual exposures) will be raised in the discussion of urinary arsenic model evaluation, Part 5.

Comment 44: The water concentrations are below levels of health concern. Additional monitoring to enhance statistical analysis is unnecessary (See Comment 35).
The cited statement was meant to address the disparity in exposures estimated for Deloro (based on a relatively high detection limit) versus Ontario. This has been addressed in recent monitoring, and supports the conclusion that drinking water in Deloro is safe.
ACTION ITEM: The report will reflect the new results based on recent analysis of municipal drinking water, including pathways analysis, and recommendations sections.

Response to Comments Provided by Dr. Charles Abernathy, United States Environmental Protection Agency

Comment 1: The number of residents for each villareis [sic] small for and epi study and it is difficult to figure out the length of exposure. These factors add some difficulty in the interpretation of the results. With that said, there really did not appear to be any differences.
Agreed there are difficulties in attempting to conduct epidemiological study of Deloro residents. As the reviewer notes, there were no significant differences between Deloro and control communities.

Comment 2: Bioavailability of As in soil. If the As species of interest are insoluble, very little is usually bioavailable. That possibly could have been the case in Deloro. A similar scenario for gardens?
Based on the results of the studies of uptake into plants, it is likely that arsenic in Deloro soils is in a less soluble, and thus less bioavailable form.
ACTION ITEM: This will be incorporated into discussion of uncertainties re: bioavailability of arsenic.

Comment 3: Standardization of urine sample using creatinine. I would have felt much more comfortable if the urine samples were palced [sic] on a creatinine basis.

While it is agreed that standardization of urinary arsenic on a creatinine basis is beneficial in interpretation, as discussed above, GGI provided rationale for evaluation on a ug/L basis.

Comment 4: Levels of selenium - Known to be a factor in the expression of As effects.
It is true that there are interactions between selenium and arsenic; however selenium did not emerge as a chemical of concern in Deloro.

Comment 5: Skin cancers - As induces a specific kind of skin cancer. It would not appear to be likely that just examining case records for skin cancers would be of much use in determining "As-induced skin cancers".
Agreed that arsenic causes a specific type of cancer (basal/squamous cell carcinoma); the review of the incidence of non-melanoma skin cancers (which includes basal/squamous cell carcinoma) was meant to help put the predicted risks into perspective only.

Comment 6: References should be included in document.
References are included at the end of every Part.

Response to Comments Provided by Dr. Christopher Le, University of Alberta

Comment 2: The fact that only single samples of well waster and municipal water were tested for arsenic is confusing. Furthermore, levels in municpal water of 5.1 ug/L in 1994 and < 10 ug/L in 1998 are reported. However, the authors claim that using a concentration of 5 ug/L is an overestimate, which would be lowered with subsequent analysis with a better detection limit (page 5-64). This assumption should not be made without further testing, since the only detected value was greater than 5 ug/L.
This issue has since been resolved through re-analysis of municipal drinking water in Deloro, which indicates a concentration of arsenic of 3.6 µg/L.

Comment 4: On page vi of the executive summary and on page 3-6 of the exposure assessment it states that direct soil exposure pathways are negligible. But in later sections of each report it is stated that dermal exposure to dust and soil contributes 10% of total exposure to arsenic, a significant amount. This should be clarified. The number of conservative assumptions used to calculate exposure for this pathway probably resulted in a proportionally large overestimation of exposure to arsenic. It is unlikely that dermal exposure exposure to soil and dust is that importation relative to ingestion of food and water.

The difference noted by the reviewer is based on the results of the deterministic analysis, which indicated that soil/dust pathways accounted for about 10% of exposure, and the results of the probabilistic analysis, which indicated that 2 to 4% of overall exposures could be traced to soil/dust pathways.
ACTION ITEM: This will be clarified in the executive summary and in the main report.

Comment 5: On page 4.2-18 of the exposure assessment, the authors make reference to

results by Le et al. (1994) and conclude that consumption of seafood may interfere with exposure assessment through urinary arsenic analysis. The results presented in this paper were due to the apparent metabolism of arsenosugars, a class of organic arsenic compounds, in the human body. This resulted in an increase of speciated arsenic in the urine from an organic source. However, this is the only time the authors consider the result. This experiment has since been further confirmed, relating consumption of bivalves (e.g., mussels) containing arsenosugars to higher-than-expected speciated arsenic in urine (Le and Ma, Analytical Chemistry 1998, 70: 1926-33). On several occasions, the authors refer to organic arsenic compounds as non-toxic and of no concern to human health. While the information provided in these sections is generally correct, the omission of arsenosugar metabolism is noticeable. These discussions should account for these recent advances in arsenic metabolism.

It is agreed that arsenosugars and their metabolism is an important aspect of exposure of human populations to arsenic-containing compounds. As noted, Le et al. (1994) observed an increase in urinary speciated arsenic following consumption of arsenosugars in the form of seaweed and bivalves. For the current assessment, this route of exposure is not expected to be significant, given that the diet of a typical Ontario resident would not include significant proportions of seaweed or marine bivalves.

ACTION ITEM: This issue will be discussed in more detail in the report, with attention to the sections pointed out by the reviewer.

Comment 7: Page 3-6, paragraph 2, line 2 of exposure assessment: "organic arsenic species are rapidly metabolized and eliminated by the body and are generally of low toxicity to humans (reference to Le et al.,. 1993, 1994). This is incorrect; it is because most organic arsenic compounds are not metabolized to any great extent that they are excreted without any health effects. This is mentioned later in the report (page 4.2-8).

It is agreed that organic arsenicals are excreted mainly in an unmetabolized form, as is stated in the main report (Section 4.2).

ACTION ITEM: This will be corrected in the Technical Summary.

Comment 8: There was no correlation observed between urinary arsenic levels and reported health effects for the citizens of Deloro. However, urinary arsenic levels assess short-term exposure only and may not correspond to potentially higher chronic exposures in the past. These prior exposure may have contributed to either observed health effects or those considered in the epidemiological study (like cancer). This is a concern in particular since high levels of contamination were observed in the 1970's. The authors also stated there was no correlation between length of residence in Deloro and health effects, which might be a more useful comparison.

It is agreed that urinary arsenic measures short term exposures, and represents a snap-shot of exposure over approximately 3 days prior to sampling.

ACTION ITEM: This would be more applicable to the Technical Summary and Goss Gilroy report, but the discussion of the importance of the urinary arsenic results will include this caution.

Editorial Comments:
ACTION ITEM: These comments will be addressed.

Comment 9: Given the depth of review for arsenic toxicity and its mechanisms of action, there is relatively little discussion of the implications of genetic differences on individual susceptibility within and between human populations. The review identified a number of biological functions which are known to be variable in people with different genetic makeups, including methylation, activity of cytochrome P450 and other enzymes related to DNA damage, generation and control of oxygen radicals in the body, and DNA repair. Although there is a brief discussion of genetic susceptibility this background is no applied to the discussion of health risks to Deloro residents. The literature suggests that for environmental exposures to carcinogens, individual susceptibility to the effects may be of similar or greater importance than the actual level of exposure. Although this type of analysis is not practical for the current study, the concept could be discussed in relation to the range of predicted effects and statistical analysis in the risk assessment. This could also be presented briefly in the Technical Summary. Susceptibility, particularly due to genetic differences between ethnic groups, could also be included as a possible reason for the conflicting results observed in the Taiwan and Utah studies.
ACTION ITEM: The importance of genetic variation will be brought forth from the toxicological profile into the discussion of results in the main report.

Comment 10: Although dermal exposure to arsenic in water through bathing would be insignificant when compared to ingestion pathways, it would be useful to mention this fact in the discussion of exposure pathways in both reports. Some readers might wonder why dermal exposure was considered for soil but not for water. Related to this is the fact that in Appendix A (Terms of Reference) of the Technical Summary, as well as in figure 5-2 of the exposure assessment, showering is mentioned as an exposure pathway, but only for the inhalation exposure to aerosols. This pathway is not addressed anywhere in the text of the report.
It is agreed that a clear discussion of rationale for inclusion and exclusion of exposure pathways should be included.
ACTION ITEM: The discussion of exposure pathways will include the rationale for exclusion of the bathing/showering pathway from the risk assessment.

Comment 11: On page 5-15 of the Technical Summary and on page 5-44 of the exposure assessment, it is stated that trespassing on the mine site only caused a significant increase in the maximum exposure values for arsenic. Mean predictions for arsenic, mean or maximum predictions for other chemicals did not increase significantly. It is then suggested that the observed increase in risk is likely overestimated for several reasons. However, the conclusion is made that trespassing would contribute significantly to exposure - this contradicts the information in this section. This conclusion was reached through the expertise of the authors, but their reasons should be explained. I do agree that restrictions on the mine site would be a logical, cost-effective risk management option.
It is true that the trespassing scenario only caused significant increases in exposure at the

maximum exposure estimate, and while we feel that this is likely overestimated, it is possible that if residents spend time at the more contaminated areas, or if they spend much more time than is anticipated on the site, there is potential for the exposures associated with trespassing to increase risks to residents. Thus the conclusion was made that trespassing may significantly to exposure, and that steps to limit these exposures should be taken. This is still held to be the most prudent course of action, although as stated, it is not believed that the site poses a significant risk to residents, the possibility does exist, and therefore should be mitigated by controlling access to the site.
ACTION ITEM: A better explanation of the above will be added to the text.

Comment 13: Throughout the Technical Summary, reference is made to "speciated" arsenic concentrations in urine samples. It is not indicated what species were determined, except "inorganic arsenic and its metabolites". Although these species (As(iii), As(V), MMA, DMA) are identified in the exposure assessment, they should be mentioned briefly in the summary document as well. These four species are listed in the glossary of terms in Appendix B of the summary report, but never occur in the text.
Agreed.
ACTION ITEM: The definition of speciated arsenic will be added to the Technical Summary, and to other relevant parts of the report.

Comment 14: The discussion on page 3-5 in the exposure assesssment about the percentage of inorganic arsenic in various food types might be misleading to some readers. It seems to imply that dairy products and meats provide the greatest concern to human health because of the high percentages listed. This should be clarified with a statement comparing the total arsenic content in each food type (refer to Table 3-4), which must be considered along with the percent inorganic arsenic.
Agreed.
ACTION ITEM: A clarification will be made as was suggested by the reviewer.

Comment 15: On page 5-9 of the Technical Summary, the following statement might seem contradictory to some readers and should be clarified: "With the consumption of homegarden produce, ER values increased minimally for Deloro residents (less than 1.2-fold); howeever, home garden produce (fruit) was considered to contribute a significant fraction of over all risk, increasing the ER above 1.2-fold over background":
Agreed.
ACTION ITEM: Clarification will be made.

Recommendations for future study:
I agree with the recommendation of the authors to obtain better estimates of arsenic concentrations in drinking water. This is a logical first step, eliminating the need for water treatment if the concentrations are close to background levels. However, this outcome should not be assumed.
Gardens from which vegetable samples were collected (6 gardens) were not in the most contaminated areas of the village. A more representative sampling and analysis of garden

soil and vegetable/fruit arsenic concentrations would reduce uncertainties associated with these parts of the assessment.

In particular, the determination of total and speciated levels of arsenic in food, such as home-grown fruit, would be useful. Risks associated with fruit are based entirely on assumptions and extrapolations; actual data would complement the results from the model. The model described on page 5-19 of the exposure assessment for estimation of dietary intake via consumption of home-grown produce is very complex, with a number of assumptions. Was there any attempt to compare these results with information from interviews of residents regarding levels of consumption? The authors suggest this is a possible course of action if fruit concentrations are found to be high.
Additional sampling and analysis of urinary arsenic using a method with a better detection limit is suggested to validate the model used to calculate expected values.
Several of these recommendations have been addressed in the time since the draft report. These include sampling and analysis of municipal drinking water with a more suitable detection limit, and identification of soil data pertaining to backyards and/or gardens (ie., present or future areas which could be used for gardening fruits and vegetables). While efforts to determine more realistic consumption values for home-grown fruits and vegetables would reduce some of the uncertainty in the assessment, the methodology used is considered to have provided a conservative estimate of daily consumption rates. In addition, for all metals except lead, the home garden produce exposure pathway had only a marginal impact on overall risks, thus refinement of consumption rates, whether increasing or decreasing, would have minimal impact on risks as well.

Response to Comments Provided by Dr. Willard R. Chappell

Comment: A very good point is made page 5-49 in the CANTOX document that the current prevalence of skin cancer in Ontario is 1/2000 from all causes. This is of course the result of the very controversial carcinogenic potency factor from U.S. EPA. This causes all the carcinogenic calculations for arsenic to take on a surreal appearance. This coupled with the RfD raises flags that should be raised. The RfD problem is more easily taken care of. If Health Canada has a higher number than U.S. EPA as stated on page 5-51 of the CANTOX document, then why no use that. Surely it has more regulatory and policy relevance to Ontario that does the U.S. EPA number. You may, by now, have the impression that I think the estimated risks are overly conservative and indeed that is the case. Again, having the EPA number for cancer causes problems. One way to help alleviate these is to emphasize over and over the conservative nature of these parameters. In fact EPA has an official statement that usually accompanies their discussion of risk assessment which goes something like "the true risk is not likely to be greater than the estimated risk and could be zero."

- Because the US EPA RfD for arsenic is more conservative, it will be retained in the assessment, however a discussion of the Health Canada value and its implications, as well as the implications of the uncertainty factors used in the U.S. EPA RfD derivation will be included in the report.

- Regarding the U.S. EPA cancer slop factor for arsenic: it is agreed that this value is highly conservative, and more emphasis will be placed on this, including a discussion of the EPA's statements in their profile on arsenic regarding the tendency of this slope factor to overestimate cancer risks.

Comment: I think more emphasis should be placed on the urinary arsenic results which clearly show no excess exposure to Deloro residents compared to controls. I would check back on the residents that were outliers for total and inorganic arsenic. It could be that the ones with high total arsenic had seafood before their sample was taken and didn't tell the interviewers about it. That is not unusual. Also, especially for the speciated samples that were high, these could be due to analytical errors. These analyses are not easy, and there could also be problems with sample treatment and preservation. I think it is always a good idea to take another sample for confirmation before telling people to contact their physician. Especially since few physicians would know anything about chronic arsenic poisoning.

- It is agreed that the fact that there was no significant difference in the urinary speciated arsenic levels between Deloro and Havelock is very important, and in the weight-of-evidence assessment, provides strong support for the results of the risk assessment in showing that Deloro residents are not experiencing significantly elevated exposures to arsenic.

Comment: A real problem exists with the drinking water because of detection limits. A part of the problem arises because ½ the detection limit for the Ontario resident is one fifth that for the Deloro resident. This is another surreal result. It is unfair to take this approach unless you analyze waters from both places using the same detection limit and, preferably, the same method. Until the water from Deloro is measured with a method that has the detection limit of 1 microgram per liter, I would consider this a "screening" risk assessment.

- The issues regarding drinking water analysis have been addressed through re-analysis of municipal water, yielding a arsenic concentration of 3.6 µg/L for Deloro drinking water.

Comment: Since the food and home garden consumption plays a big role I think that extensive sampling of fruits and vegetables is warranted. I don't like the BTF approach. There are all kinds of problems with the underlying assumptions of linearity, etc. It would be far better to actually measure the arsenic concentrations in the food and then, by survey, or some other method, estimate the consumption rates for the various foodstuffs.

- It is agreed that actual sampling and analysis of food stuffs would provide the best estimate of concentrations to which consumers are being exposed; however, within the scope of the current assessment, the analysis of vegetables from Deloro gardens, and the development of site-specific BTFs based on these analyses, is considered appropriate and scientifically defensible.

Comment: I believe the dermal absorption for arsenic is much over estimated. I think you said Buck Grissom from ATSDR is a reviewer. I will defer to him as the expert.

- The dermal absorption for arsenic and the other metals likely has been overestimated, in that when there was any uncertainty regarding a parameter such as dermal adherence, emphasis was placed on selecting conservative but realistic values.

Comment: In the discussion about skin lesions in children on page 5-50 in the CANTOX report, I would note that in India where the water concentrations are very high, up to 4 mg/L, they do not see skin lesions in children less than 11 years old, let alone infants. In Banglasdesh there have been some reports for children under 11, but it is suggested that this is due to poorer diets (although this is not proven). Even there they have not seen the skin lesions in infants. I would de-emphasize this issue because it worries people unnecessarily. If you use the Health Canada RfD this problem will go away.

- Regarding the issue of skin lesions in children: It is true that the risk of developing skin lesions sharply increases at ages above 20 years, and thus the application of the RfD, which is protective of development of skin lesions in adults, to exposure rates of children is considered to be highly conservative. The reviewer's point that such skin lesions are rarely seen in children under 11 years of age is well taken; the risk estimates would be dependent on the exposure to arsenic for a lifetime, with onset of symptoms really only possible in adults. In addition, the use of the Tseng *et al.* studies in the derivation of the non-cancer criteria has many of the problems associated with its use in the cancer slope factor derivation (uncertainty and likely underestimation of actual dose levels by failing to account for food, medicinals, etc., and poor nutrition). As suggested by the reviewer, the issue of skin lesions will be discussed in the context of the above information and in the context of the Health Canada exposure limit for non-carcinogenic effects.

Comment: I don't think the appropriate procedure was used for indoor dust sampling. The wipes and dust fall methods are not as good as a method we used in a study in Colorado and has been used elsewhere. This involves the use of a small pump (basically it is a personal air monitor sampler turned into a mini vacuum cleaner) to pull dust into a filter. Another method some people use is to collect dust from household vacuum cleaners. This gives enough sample to get "detects" and gives the concentration in the dust as micrograms As per gram of dust. Then you don't need to worry about hand surface area, etc. and can use information on dust ingestion in mg/day. But I don't think this needs to be redone because it didn't have much significance.

- The uncertainties and limitations of the indoor dust data, as presented to CANTOX ENVIRONMENTAL were such that the provided data were not employed; rather, exposures via indoor dust were based on the relationship (based on those developed by Huang *et al.* and Calabrese *et al.)* describing the ratio of concentrations in dust in indoor air and outdoor soil.

Comment: The trespasser scenario is too conservative. The assumption of spending 0.5 hour per day at maximum concentration doesn't make sense. A better approach might be to

weight the time spent by the area, so that if the maximum concentration was for only 1/100th of the area then 1/100th of the time spent trespassing is at that concentration. Even that is probably too conservative as I expect that the highest concentrations are in areas that are either relatively inaccessible or not very appealing.

- It is agreed that the trespasser scenario is conservative.

Comment: While I enjoy doing Monte Carlo estimates, it is not clear how useful this one is. Especially since most people won't understand it anyway. However, I would not have used the triangular distribution for everything. We know that most distributions for concentrations are lognormal so one approach would be to fit a lognormal distribution to the data. However, an even better use of all the data would be to either fir the data or to use a cumulative distribution. Spreadsheets can give you the percentile values and then programs like @RISK have the ability to put in these percentile values and use a cumulative distribution. Either approach makes use of all the data rather than just some of it. My guess is that the triangular distribution over estimates the risk because it doesn't give enough weight to the values less than the mode for a lognormal-shaped distribution.

- The use of triangular distribution for representation of the data was thoroughly researched and tests of Goodness of Fit indicated that this was most appropriate; Log Normal relationships failed several major tests of goodness of fit, and were thus rejected as appropriate for use in representing the data. It is acknowledged in the report that the use of triangular distributions would be conservative, but again, in absence of defensible alternatives, conservative methods were employed throughout the assessment.

Response to Comments Provided by OMOE personnel

Comment 1: Cantox Environmental Inc. communicates that "background" values for the metals of concern in the Deloro Environmental Health Risk study often approach or exceed the Exposure Ratio (ER) value designated as the benchmark of safety. This implies that most communities in Ontario are, through a variety of pathways, exposed to concentrations of metals that exceed "safe" levels.
Are these unsafe predicted background levels "real" (are they supported with measured values) or do they suggest problems with toxicological overestimates. When discussing the relevance of U.S. EPA potency estimates for oral exposures to arsenic, Cantox notes that "There has been considerable discussion of the shortcomings of these studies, specifically in regard to their applicability to the much lower doses commonly experienced by typical North American populations".
As discussed in the document, it is not expected that "background" exposures are associated with elevated risk, rather, when elevated risk levels are indicated for background or typical Ontario residents, it is an indication of over-conservatism in the risk assessment.

Comment 2: The report concludes that fruits are a significant contributor of arsenic through the oral pathway. I believe that conclusion is based on a single apple tree that was sampled within the community of Deloro. The limited availability of data associated with fruit crops

should be stressed when these findings are communicated.
The original analysis relied on a very conservative assumption - the extrapolation of BTF from vegetables to fruit; this has since been replaced by a BTF from the literature which related soil concentrations to those observed in apples from trees grown in those soils. As might be expected, the concentrations in the fruit decreased, and the significance of this pathway has decreased as well.

Comment 3: It is indicated that root vegetables contributed approximately 60 to 70% of the maximum and 30 to 40% of the mean overall risk for lead. Since the report seems to conclude that the predicted Exposure Ratio value for Deloro residents with respect to lead is not appreciably different than the background level it serves little purpose to identify root vegetables as a significant contributor to lead exposure.
Root vegetables comprised a major portion of the exposure from home garden produce, and the inclusion of this fact in the examination of contributors to overall exposure seems appropriate.
ACTION ITEM: It will be emphasized that despite this importance, the consumption of home garden produce is not expected to result in measurably increased risks associated with lead.

Comment 4: The communal water supply is cited as a significant source of arsenic exposure yet it is noted that concentrations of less than the detection limit contributed to "uncertainties" in the health risk analysis. I am very concerned about casting dispersions on the quality of the communal water supply. The water works has been consistently demonstrated to conform with every water quality standard stipulated in the Ontario Drinking Water Objectives.

I suggest that statements linking the communal water supply to significant arsenic exposures be removed unless it can be demonstrated that the drinking water supply definitely contains "measurable" concentrations of arsenic and that those concentrations pose a health risk.
It is agreed that the municipal water in Deloro is within the Ontario drinking water objectives, and is not considered to pose a health concern to residents; rather the significance of the drinking water contribution merely emphasizes that the cancer slope factor promulgated by U.S. EPA is extremely and probably overly conservative.
ACTION ITEM: this will be clarified in the report.

Response to Comments Provided by Murray Dixon, OMOE

In the document entitled "Deloro Village Health Risk Study - Overall Technical Summary Draft Report" on page III, at the end to the Garden Soil section, and on page 2-2 under Findings, it is stated "It should be noted that the selected gardens were not located in the most contaminated areas of the village". This statement could be interpreted to mean that gardens in the most contaminated areas of the village were not selected, which was not the case. Wording such as "The selected gardens represent contaminated areas of the village" presents a more accurate representation of the situation. When we collected the soil samples

from the residential properties in Deloro we noted any gardens. Only one garden was noted that was not used and this garden was only 1 x 2m in size, had been used a play garden by the owners daughter, was not going to be planted in 1998 and the house was for sale.

Also on pate 2-2 of the overall Technical Summary Draft Report under the heading (Soil) Findings, the phrase "for cobalt" was omitted. It should read "Maximum concentrations were 605 ug/g compared to guidelines of 25 ug/g for arsenic; 340 ug/g compared to guideline of 50 ug/g for cobalt. Finally, the contour maps in Appendix D have been revised. I have sent you the revised Phyto report, which includes the revised contour maps.

I feel the risk estimate for consumption of garden vegetables is extremely conservative. In the main CANTOX document, Deloro Village Exposure Assessment and Health Risk Characterization for Arsenic and Other Metals, Part 5, Section 2.6, they give the rationale for their approach to estimating contaminant concentrations in home grown produce. Although the approach is logical, the reality is that very few people in the village grow vegetables. The big gardens tend to be in the north end of Deloro out of the area of highest contamination. As you know it was difficult coming up with 7 gardens, and of the 7, tow were gardens planted because we requested a garden.

We agree that the estimation of consumption via the home garden was conducted in a conservative manner, including the estimation of daily intake of fruits and vegetables, as well as in the assumption that gardens could be located anywhere in Deloro.
ACTION ITEM: The conservatism in the assessment of exposure through consumption of home garden produce will be emphasized, and since data regarding concentrations of metals in backyards and garden plots (i.e., where gardens are or might be located) has become available, the maximum risk estimates will be discussed in terms of overestimation of soil concentrations and thus fruit/vegetable concentrations.

Additional comments:

1. Executive Summary, Page v:
The second sentence says that "the threshold approach applies to the non-carcinogenic effects of a metal. No adverse effect will occur until some threshold dose limit...is exceeded." This is the standard traditional conceptual approach which implies that the RfD changes depending on the sophistication of the testing to identify an adverse effect; if fact, how an "adverse effect" is defined is entirely arbitrary.
Agreed.

2. Page 3-2, 4th paragraph under Urinary Arsenic Results:
My concern here is similar to the one above. The fact that non of the five respondents showed any adverse health effect based on their responses to the health risk questionnaire is very hard to interpret because it depends on how sensitive the questionnaire is (i.e., whether the "right" questions were asked) and how the respondents interpreted the questions (NB: I have not seen the questionnaire and I don not know how it was administered so this concern

may not be valid).
Agreed.

3. Page 5-12, last paragraph:
The "acceptable blood lead level (PbB)" should be 10 ug/dL, no "10g/dL"
Will be corrected.

4. Appendix C, page 6, 4th paragraph under Summary/Key Considerations:
Second sentence has too many "not"s – "It is not therefore not comparable..."
Will be corrected.